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THE EFFECTS OF ASPHYXIA ON THE NEWBORN INFANT

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THE human fetus is particularly vulnerable to any interference with its normal oxygen supply. Asphyxia of the fetus may initiate a chain of physiologic and pathologic changes affecting every organ and tissue in the body and resulting in a wide variety of otherwise unrelated clinical symptoms in newborn infants.

Asphyxia is probably the most important single cause of disease and death in newborn infants. It is being recognized increasingly as being responsible for many neurological changes manifest in older age groups. Asphyxia was found to be the chief cause of death in 58 per cent of 284 liveborn infants autopsied at the Boston Lying-in Hospital since 1931.

GENERAL REVIEW OF PHYSIOLOGIC AND PATHOLOGIC EFFECTS OF ANOXEMIA

The fundamental effect of anoxemia is the production, through an accumulation of carbonic and lactic acids, of an increased hydrogen-ion concentration in the body.[1, 7] The first change that takes place in the blood as the result of anoxemia is an increase in its carbon dioxide content.[2, 6, 7] Carbon dioxide is a more effective stimulant than other acids because of its power of rapid diffusion and great penetrability.[1, 2, 7] With continued oxygen lack there is interference with the process of cell metabolism resulting in the production of lactic acid.[1, 6, 7] The effects of severe asphyxia are primarily due to this accumulation of lactic acid[8] that may reduce the pH of the blood to a point incompatible with life.[9]

The central and peripheral effects of an increased hydrogen-ion concentration are in opposite directions.[1] On nerve cells the hydrogen-ion produces the progressive states of excitation, discharge of energy,

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and finally exhaustion or paralysis.[7] On cardiac muscle an increased hydrogen-ion concentration produces loss of muscle tone and dilatation,[5] while on blood vessels it results in loss of muscle tone,[4] dilatation,[1, 4] liberation of plasma,[10] and hemorrhage.[10]

Anoxemia exerts a combined effect on the blood vessels and individual cells of the nervous system. The loss of muscle tone and dilatation of the smaller blood vessels and capillaries result in the loss of plasma, perivascular edema, the packing of vessels with red cells, and hemorrhage.[11, 12] The slow blood flow resulting from the packing of red cells in the vessels may produce conditions resulting in thrombus formation, eventual fibrous obliteration of vessels, and possibly permanent depletion of blood supply to small or large areas.[10, 12] With the onset of asphyxia the increased hydrogen-ion concentration first produces an excitation of the various centers including that for respiration. With continued anoxemia these nerve cells may pass through the successive phases of discharge of energy and paralysis. The two processes just described are closely related as the vascular changes and edema add to the degree of local tissue asphyxia.[11]

"The vessels of the brain are especially sensitive to an increased hydrogen-ion concentration and congestion of cerebral vessels, cerebral edema, and increased cerebrospinal fluid pressure occurs even in cases of mild carbon monoxide asphyxia and is very severe in prolonged fatal cases."[10]

The heart rate in asphyxia is first increased, presumably through a stimulation of the cardiac centers. Stimulation of the vasomotor center then follows producing arteriolar constriction and a marked rise in blood pressure.[1, 6] The heart rate is then slowed as a result of the increased blood pressure[1] combined with the hydrogen-ion stimulation of the cardio-inhibitor center and sinoauricular node.[3] The hydrogen-ion action upon auriculoventricular conduction may produce extra systoles, irregularities in rate, and even heart block.[1, 3] As the pH of the blood falls with continued anoxemia the heart, small veins and capillaries lose their tone and undergo dilatation,[1, 4, 5] the blood pressure falls, and the heart eventually fails as the result of local oxygen lack.[1]

In asphyxia (caused by carbon monoxide) "the smaller blood vessels apparently become fragile, and hemorrhages, varying from minute to fairly large, may be found in many parts of the body. The peritoneum and omentum may show many fine hemorrhages. Similar hemorrhages may be seen under the mucous membrane of the respiratory and gastrointestinal tracts, and over the surface of the heart, lungs, pleura, and pericardium. Of especial importance are the fine hemorrhages in the brain and meninges. There can be little doubt that these hemorrhages express the direct effect of extreme degrees of oxygen lack upon the smaller blood vessels."[10]

"In considering abnormal degrees of vascular permeability, it must be understood that two types of effect may be expected: First of all,

an increase in the fragility of the vessel walls, which permits actual leakage of red cells and even small hemorrhages; and second, a more general effect which leads to abnormal leakage of the blood plasma without actual escape of red cells. Prolonged severe asphyxia will have this latter effect. It is expressed in accumulations of fluid in the peritoneal, pleural, and pericardial cavities."[10]

ACTUAL CLINICAL AND PATHOLOGIC CHANGES OBSERVED IN NEWBORN INFANTS FOLLOWING INTRAUTERINE ASPHYXIA

A group of eleven newborn infants have been selected for study from 164 who met asphyxial deaths as representing the clinical and pathologic changes that may be produced by intrauterine asphyxia. In all eleven patients the fetal anoxemia had been produced by the separation of a low attached placenta (placenta previa) accompanied by active hemorrhage present just prior to birth. All patients had been delivered by cesarean section, performed before the onset of labor, as being the quickest and safest method of terminating the intrauterine fetal asphyxia. No mother had received any preliminary obstetrical analgesia before operation. No infant showed any autopsy evidence of traumatic intracranial injury as evidenced by rupture of the vein of Galen or significant tears in the falx or tentorium. No infant showed any congenital anomaly that might have affected its course. And, finally, for each patient complete obstetric, pediatric, and autopsy records were available for study.

CLINICAL FINDINGS

Of the eleven infants in this series, six were in poor condition from birth and lived four to thirty-six hours. These infants exhibited respiratory distress from birth with labored, grunting breathing, dilatation of the alae nasae, and marked retraction of the costal margins. They were subject to periods of apnea and to varying degrees of cyanosis; their cries were feeble; their reflexes were absent; and their muscles were hypotonic. The majority showed petechial hemorrhages and subcutaneous ecchymoses. One infant vomited blood, and two developed tense and bulging anterior fontanels, later shown to be due to a marked accumulation of clear cerebrospinal fluid. Another infant, whose fontanel was not recorded as abnormal in life, had an accumulation of clear cerebrospinal fluid over the cortex to a depth of 2 cm. at autopsy.

Of the eleven infants, three were considered to be in fair condition for several hours following their resuscitation at birth, except for grunting respiration and cyanosis of the extremities. Severe respiratory embarrassment then developed, accompanied by retraction of the costal margins and recurring attacks of generalized cyanosis. One infant developed petechial hemorrhages in the skin with scleroderma; a second

baby became spastic and developed convulsive twitchings later shown to be due to a massive intraventricular hemorrhage, while the third infant passed several bloody stools and had bleeding from the nose. These three infants died between the ages of 6 and 36 hours.

The remaining two of the eleven infants breathed spontaneously at birth and were considered to be normal for several hours. They then developed the same syndrome of respiratory distress characteristic of the rest of the group. One infant had respirations ranging from 60 to 120 per minute with periods of apnea lasting ten to sixty seconds and bleeding from the nose and mouth and into the subcutaneous tissue of the thorax before his death at 12 hours. The second infant developed labored respirations at 2 hours of age; at 17 hours the respiratory distress was marked, but the anterior fontanel was normal; at the age of 2 days the fontanel became full; at 3 days the fontanel became tense, and apnea, cyanosis, sclerema, and generalized muscular rigidity developed. Lumbar puncture produced a bloody cerebrospinal fluid containing 50 per cent crenated red blood cells. This baby died at the age of 6 days. Among other findings, the autopsy showed hemorrhage in the subarachnoid space, hemorrhage into the ventricles, and an extreme degree of encephalomalacia.

PATHOLOGIC FINDINGS

Skin and Subcutaneous Tissue.—Edema was present in six infants: in the extremities in three, in the thoracic subcutaneous tissue in one, in the scalp in two, and in the scrotum in one. In six cases petechial hemorrhages or subcutaneous ecchymosis were recorded.

Body Cavities.—Table I gives the amounts of clear amber fluid found in the various body cavities.

TABLE I

CASE NO.	BIRTH WEIGHT (LB.)	PERITONEAL CAVITY (C.C.)	PLEURAL CAVITIES		PERICARDIAL CAVITY (C.C.)
			RIGHT (C.C.)	LEFT (C.C.)	
1	3-8	3	Small amount	Small amount	2
2	3-11	0	0	0	2
3	4-7	10			0
4	4-8				1½
5	4-11	Trace	0	0	Small amount
6	4-12	2			
7	4-14½				2
8	5-7	Normal	0	0	2
9	5-13	0			4
10	6-14½	Small amount*	Small amount	Small amount	Small amount
11	9-3	20	10	10	5

*In this case a large amount of retroperitoneal edema fluid was found.

The Heart (Gross).—In all patients the epicardium showed moderate to extreme blood vessel congestion. In seven infants epicardial and sub-

epicardial hemorrhages were found, varying in size from scattered petechial hemorrhages to extravasations measuring 1.5 cm. In four instances the heart appeared enlarged, one due to dilatation of the right auricle and ventricle and one due to hypertrophy of the left ventricle; in two cases the enlargement was generalized. In one infant the endocardium contained an occasional petechial hemorrhage while in two others blood cysts were found in the leaflets of the tricuspid valve.

The Heart (Microscopic).—In ten infants the epicardial blood vessels were described as moderately to intensely engorged. In one infant the epicardium showed mild edema; three infants showed occasional small areas of epicardial hemorrhage; one child had a small area of hemorrhage dissecting through the epicardium forming an extravasation of blood in the myocardium; and another patient had a large amount of hemorrhage throughout the epicardial stroma. In five infants the myocardium showed slight edema; in four there was intense blood vessel congestion extending to the myocardial capillaries; in one infant, mentioned above, a myocardial hemorrhage was present, while in another the intramuscular tissue of the myocardium was loose and edematous and contained occasional laked red blood cells.

The Lungs (Gross).—The lungs of only one patient were described as moderately well expanded, retaining their relationship to the pericardium and mediastinal structures. In the remaining ten patients the lungs were almost completely collapsed and retracted from the chest wall. The little expansion present was found uniformly in the anterior margins and occasionally in the central lobules. The visceral pleural surfaces over the expanded portions had a pale pink color. Emphysematous blebs were found over the small areas of expanded lung in the infant living six days. The unexpanded areas had a deep reddish purple color. Numerous petechial hemorrhages were seen over the surface in six infants. Crepitation could be felt over the expanded margins in six, while the rest of these lungs were reported as firm, meaty, or rubbery. In five infants no areas of expansion could be felt, and the lungs were described as solid.

The cut sections showed the expanded portions as pinkish, producing a frothy hemorrhagic fluid on pressure. The bulk of the lungs was deep red or bluish red, producing only dark fluid blood on pressure. Sections of these latter areas sank in water. The trachea and bronchi contained frothy material for the most part with no gross evidence of meconium or vernix plugs.

The Lungs (Microscopic).—In all infants marked blood vessel engorgement extending to the alveolar capillaries was present. In four infants the pleura was described as edematous; in six infants pleural hemorrhages were found, and in five of these the blood had dissected below the pleura along the connective tissue and into the lung stroma. A massive hemorrhage occupied a portion of one lung, giving it the ap-

pearance of liver tissue. Numerous areas of hemorrhage were encountered throughout the parenchyma in two others.

The alveolar walls showed intense capillary congestion with occasional monocytic, polymorphonuclear, and macrophagic infiltration and occasional areas of hemorrhage. In five infants in alveoli contained either edema fluid or a bright pink staining material at times forming a complete hyaline membrane along the alveolar walls. In two of these keratinized epithelial cells were encountered in the alveoli. In the remaining six infants the alveoli contained a varying amount of blood in addition to the edema fluid or to the hyaline material. The alveolar blood content varied from occasional red blood cell ghost forms to true alveolar hemorrhages with asphyxia membranes formed of red blood cells. In one of the latter vernix was found in the alveoli, but almost as conspicuous were the marked congestion and hemorrhage.

In seven infants the alveolar ducts were cystically dilated and lined with asphyxial membrane. In three infants the dilated ducts contained keratinized epithelial cells, and in one of these the epithelial cells were intermingled with red blood cells.

In the lungs as a whole, no evidence of aspirated meconium or vernix could be found in five infants; occasional keratinized cells were reported in three; and moderate to marked evidence of aspirated amniotic fluid was found in three.

The Spleen.—The spleens had a dark purplish color with one showing numerous petechial hemorrhages beneath the capsule. Microscopically all showed moderate to intense vascular congestion. Three showed marked extravasation of red cells into the parenchyma, while two showed a moderate to a marked number of nucleated red blood cells.

The Alimentary Tract.—In six infants the mucosa of the esophagus was markedly congested; in one infant a few petechial hemorrhages were noted; in another a large amount of bloody mucus was found adherent to the mucosa throughout its entire extent. Microscopically a third showed the tunica propria of the esophagus to be filled with extravasated red blood cells.

In four infants the mucosa of the duodenum was slightly to markedly congested; in one infant the mucosa showed the numerous points of hemorrhage on both gross and microscopic examination; in another the mucosa was covered with a bloody mucoid material.

In one patient the jejunum for a distance of 25 cm. showed a moderate amount of hemorrhage mixed with bile-stained mucoid material due to a diffuse oozing of blood from the congested mucosal surface; in a second infant the mucosa showed gross and microscopic evidence of marked congestion with numerous points of hemorrhage.

In three infants the ileum showed moderate to marked congestion on microscopic examination.

In one baby the stomach showed a large amount of hemorrhagic mucoid material and numerous areas of petechial hemorrhage in the

gastric mucosa, while in a second infant the gastric mucosa was injected but without hemorrhage.

The Pancreas.—In six infants the blood vessels of the pancreas were reported as moderately to tremendously engorged, and in six patients the stroma of the pancreas was described as being edematous.

The Liver (Gross).—In all eleven patients the livers were congested and of a mottled dark reddish brown color, with scattered, small, yellowish areas of fatty infiltration. One liver contained multiple areas, measuring 2 to 7 mm., of reddish brown softening due to hemorrhage and necrosis. One was strikingly pale in appearance due to marked fatty infiltration. In three livers there were areas of subcapsular hemorrhage, measuring 1 mm. to 1.5 cm.

The Liver (Microscopic).—In eight infants the liver vessels including the sinusoids were congested. In six infants subcapsular hemorrhages were described ranging from thin layers of red blood cells to extensive hemorrhages elevating the capsule. In one patient the liver showed marked dissolution of tissue in the midzonal areas characterized, particularly at the zone of juncture between these and preserved areas, by almost complete necrosis of liver cells and moderate hemorrhage. In five infants evidence of fatty infiltration of the liver was present. In one patient the liver showed in all areas a tremendous amount of fat in the cells, the most marked fatty infiltration being in the cytoplasm of those cells around central veins. Likewise in another patient the liver cells contained a great deal of fat and a minute amount of granular cytoplasm. In still another the liver cells presented occasional small vacuolated areas of fatty infiltration in the central part of the lobules. In seven patients evidence of erythropoiesis was present, varying from small islands of hematopoiesis to extensive erythropoiesis in three livers.

The Kidneys.—The kidneys showed little on gross examination beyond occasional petechial hemorrhage. Microscopically all showed moderate to intense blood vessel congestion. In four infants small areas of hemorrhage were found, while in two there was moderate edema of the kidney stroma.

The Thymus.—In eight patients the thymic capsule was studded with petechial hemorrhages. In four infants these hemorrhages were found throughout the parenchyma. All eleven infants showed marked engorgement of the thymic blood vessels. In two patients edema was noted in the thymic capsule, and in four infants it was seen throughout the stroma. In two infants there were extravasations of blood in the gland parenchyma.

The Brain (Gross).—In ten patients the arachnoidal and cerebral vessels of the brain were engorged and tortuous. In six the arachnoid was bulging due to a great increase in the amount of clear cerebrospinal fluid.

In one infant there was a layer of clear cerebrospinal fluid to a depth of 2 cm. over the cerebral cortex, while in another the medulla was surrounded by a thick gelatinous-like layer of clear cerebrospinal fluid. In only two infants was there evidence of gross blood in the cerebral subarachnoid spaces; in one of these a small amount of blood was diffused over all aspects of the brain, while in the other a 5 by 3 by 0.3 cm. blood clot was present over the left cerebral hemisphere, and the subarachnoid space was filled with fluid blood under tension.

In two babies the brain cortex was covered with petechial hemorrhages. In one infant the brain was markedly softened, the encephalomalacia not being due to post-mortem change. In one child there was dilatation of the lateral ventricle, while in two others the ventricles contained massive hemorrhage extending through the fourth ventricle and around the medulla. In these the choroid plexuses were incorporated in the blood clot.

In all infants the falx, tentorium, and vein of Galen were examined, and no evidence of tears or rupture could be found. In four infants a few petechial hemorrhages were seen in the falx and tentorium. In three children, although the veins of Galen were found markedly engorged, there had been no rupture.

The Brain (Microscopic).—The brains of two infants were not examined microscopically. In the remaining nine infants there was marked congestion of all the blood vessels in the brain. In seven infants evidence of cerebral edema was present. In three patients the brain showed scattered small areas of hemorrhage. In the infant with encephalomalacia, the brain showed deep congestion of all the meningeal and cerebral vessels, recent and old hemorrhage with phagocytosis and hemosiderin deposition into and below the pia, generalized edema of the brain tissue with widened perivascular spaces, petechial hemorrhages in the ganglion layers of the cortex and cerebellum, and recent diffuse hemorrhage in the lateral ventricles. In another infant the brain showed engorgement of all the cerebral vessels, cerebral edema, cerebral ganglion cell degeneration, subependymal perivascular hemorrhage in the region of the basal ganglia, marked engorgement of the choroid vessels with the stroma in this region showing edema and a considerable degree of recent hemorrhage, and ganglion cell degeneration in the region of the medulla.

The Spinal Cord.—The spinal cords of eight infants showed marked congestion, and those of four children were edematous. In two patients the cords showed subarachnoid hemorrhage, while in one patient the spinal cord showed petechial hemorrhage in the dorsal column.

DISCUSSION

The effects of asphyxia involve the organism as a whole even though symptoms referable to one part of the body, such as pulmonary atelectasis or intracranial injury, may dominate the picture. The extensive

pathologic changes and the variety of clinical symptoms found associated with asphyxia are best explained as the result of underlying physiologic changes brought about by anoxemia.

The basic physiologic effect of anoxemia is the production, through an accumulation of carbonic and lactic acids, of an increased hydrogen-ion concentration in the body. The hydrogen ion has a fundamentally different effect on nerve tissue than it has when acting on smooth and cardiac muscle. On nerve cells it induces the successive stages of stimulation, discharge of energy, and paralysis. On the smooth muscle of blood vessels and capillaries it produces loss of tone and dilatation thus allowing the escape of plasma and hemorrhage. On cardiac muscle it produces loss of tone, dilatation, and eventually failure.

The pathologic changes that have been found following intrauterine asphyxia may be summarized as congestion, edema, hemorrhage, and tissue degeneration. The *congestion* of blood vessels was profound, involving every organ and tissue and extending to the finest capillaries. *Edema* fluid was observed in the subcutaneous tissue, in the muscles of the extremities and the heart, in the periadrenal, the peripancreatic, and the retroperitoneal tissues, in the capsule and stroma of the adrenals, the thymus, the liver, and the pancreas, in the pleura, the lungs, the subarachnoid space, and the brain; and in the peritoneal, the pleural, and the pericardial cavities. Petechial *hemorrhages* were found scattered extensively throughout the various organs, while greater degrees of *hemorrhage* were found in the lung alveoli and parenchyma, the liver capsule and parenchyma, the heart, the intestinal tract, the subarachnoid space, the ventricles, and the brain substance. Actual *tissue degeneration* was evidenced in the liver by varying degrees of fatty infiltration, marked necrosis, and dissolution of tissue accompanied by hemorrhage and in the brain by changes ranging from areas of ganglion cell degeneration to widespread encephalomalacia.

The clinical symptoms that have been observed in asphyxiated infants are the result of the physiologic and pathologic changes induced by anoxemia. The actual symptoms encountered and their severity depend upon the degree and duration of the anoxia and upon the susceptibility of individual tissues.

Symptoms referable to the nervous system are the result of the combined effects of asphyxia on the blood vessels of the brain and on the nerve cells themselves. The loss of tone and dilatation of the blood vessels of the brain with escape of fluid and even blood causes intense congestion of all vessels, perivascular and cerebral edema, petechial or larger hemorrhages in the brain substances, and a great increase in the amount of cerebrospinal fluid, which fluid may contain a variable amount of free blood. These changes may cause bulging of the anterior fontanel, separation of the sutures, abnormal increase in the size of the head, convulsions, interference with respiration, cyanosis and atelec-

tasis of central origin, and gross neurological damage. The successive stages of nerve cell stimulation, discharge of energy, and paralysis affect the brain centers causing acceleration of the fetal heart, aspiration in utero, difficulty in resuscitation at birth, irregularities in respiratory rate and rhythm, cyanosis or atelectasis of central origin, muscular hypertonia or hypotonia, convulsions, and permanent neurological damage. The peripheral nerve centers likewise may be affected causing extra systoles (irregularities and slowing of the heart rate) and heart block.

The phenomena of asphyxia may be confined to the intrauterine period, and recovery may set in at birth, providing the lungs are capable of supplying an adequate supply of oxygen to the tissues. It is more common, however, to have the function of the lungs so interfered with by the fetal anoxia that they are unable to sustain a positive oxygen balance. Under these conditions the oxygen lack present in utero persists and may become more marked in extrauterine life, with the patient's clinical state becoming progressively more serious unless relief can be afforded. It is possible to have a relatively slight fetal asphyxia produce dangerous extrauterine anoxemia if by chance the fetal process seriously involves the lungs or the respiratory center.

Wilson and Farber[13] have pointed out that the cohesion of the moist surfaces of the air passages in collapsed and airless lungs offers a considerable mechanical resistance to the entrance of air and that a relatively great force is required to overcome this cohesion during the initial expansion of an atelectatic lung. When this normal resistance to expansion was coupled with (1) an injured respiratory center, (2) an imperfectly developed thoracic mechanism, or (3) bronchial obstruction due to aspiration of amniotic sac contents, mucus or blood, the state of atelectasis would be prolonged to a pathologic extent.

The above explanation does not seem entirely adequate to explain the type of atelectasis here reported. In our cases, while the factor of injury to the respiratory center was undoubtedly present to some degree, it was not sufficiently prominent to explain all the findings. Bronchial obstruction was decidedly not a factor. Another possible explanation suggests itself that is in keeping with the pathologic findings observed in other organs. In the presence of asphyxia the blood vessels of the lung undergo loss of tone and dilatation, allowing escape of plasma and red blood cells into the surrounding lung tissue and into alveoli. This process would explain the observed findings of congestion, edema, and hemorrhage in the lung stroma and in the alveoli. Thus an additional factor may be present under certain conditions preventing the normal expansion of the lung, namely, the increased turgor or resistance of the lung substance. While this hypothesis should be investigated further, it is in keeping with DeLee's statement, "We long ago gave up the notion that it is possible to inflate the atelectatic alveoli of the lungs.

In 1902 I proved that air under 3 pounds pressure would not do it."[14] Dr. Clement A. Smith of this clinic found that a much greater pressure was required to forcibly expand the lungs from an asphyxiated baby of the type here discussed than was required for ordinary infant lungs.* Our present clinical treatment of asphyxia is based on this hypothesis, and its success adds weight to the truth of the premise. We make no effort to forcibly expand the asphyxiated infant's lungs but keep him at complete rest in an atmosphere of 50 to 60 per cent oxygen. If the infant is to survive, its general condition quickly improves in oxygen, and usually by the fourth day the x-ray and physical examinations demonstrate expansion of the atelectatic areas. The point is of such great practical importance that more extensive studies are indicated.

There are numerous other clinical findings observed in asphyxiated infants that find their explanation on a physiologic basis. The liberation of edema fluid explains the findings of subcutaneous edema, sclerema, and fluid in the body cavities. The association of petechial hemorrhages with asphyxia is well known, but the importance of extensive asphyxial bleeding in other locations should be stressed. Much of the gastrointestinal, pulmonary, and liver hemorrhage may be of this origin. Asphyxia, in the complete absence of trauma, may be responsible for varying degrees of hemorrhages into the cerebrospinal fluid, into the ventricles, and into the brain substance itself.

CONCLUSIONS

Asphyxia is responsible for over one-half of the live-born infant deaths in the newborn period.

The fundamental effect of asphyxia is the production of an increased hydrogen-ion concentration that causes the successive stages of stimulation, discharge of energy, and paralysis in nerve cells and produces loss of tone and dilatation of the smooth muscle of blood vessels allowing the escape of plasma and red blood cells.

The pathologic changes induced by asphyxia may be summarized as congestion, edema, hemorrhage, and tissue degeneration. These changes may involve every organ and tissue of the body.

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*Dr. Smith's report on Baby G.'s lungs. The lungs show massive atelectasis following intrauterine asphyxia. "The lung is suspended in a jar, and is responds to the rhythmic application of negative pressure as follows (measurements in cm. of water):

1. Minus 8 cm. for 5 minutes	No effect
2. Minus 13 cm. for 5 minutes	Very little effect, about 1 c.c. of air in and out of lung with each 'breath.'
3. Minus 19 cm. for 6 minutes	First visible expansion of scattered areas of lung surfaces begins and coincidentally definite emphysematous blebs appear.
4. Minus 22 cm. for 8 minutes	Further expansion, but still not including as much as 50 per cent of the lung surface and only 3 c.c. of air per 'breath.'
5. Minus 30 cm. for 2 minutes	Lung expands, but *not* completely, and the blebs are larger. Each 'breath' is about 8 c.c.

"By contrast, Baby A-40-26, a stillborn infant delivered the same day as Baby G; showed complete expansion at minus 22 cm. of water and ventilation of about 10 c.c. per 'breath.' The cause of death in this infant was uncertain, but these figures are fairly typical of the 'normal' stillborn lung."

The clinical symptoms are those to be expected from the combined physiologic and pathologic effects of asphyxia.

The effects of asphyxia involve the organism as a whole even though symptoms referable to one part of the body may dominate the picture.

The atelectasis of the lungs seen in asphyxiated infants may be due to a combination of factors: (1) The normal resistance of expansion due to the cohesion of moist surfaces, (2) injury to the respiratory center, (3) bronchial obstruction, and (4) increased turgor of the lung tissue itself due to the congestion, edema, and hemorrhage associated with asphyxia.

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CONGENITAL MEGACOLON (HIRSCHSPRUNG'S DISEASE)

Report of a Case Treated With Acetylbetamethylcholine Bromide, With Apparent Cure

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THE search for a satisfactory explanation of the cause of congenital megacolon, a disease first described by Hirschsprung and bearing his name, has been going on since the year 1886. The theories of causation which have been offered are all based on the hypothesis that there exists an imbalance of the autonomic nerve supply of the colon. For a better understanding of the underlying disturbance a brief review of the nerve supply to that portion of the intestinal tract which is involved in congenital megacolon is presented.

The distal portion of the colon is innervated by the sympathetic nerves coming from the spinal cord at the first and second lumbar segments. The preganglionic fibers pass uninterrupted through the first and second lumbar ganglia to the inferior mesenteric plexus where it joins a branch from the intermesenteric plexus; postganglionic fibers from the former plexus go to the colon. The rectal sympathetics are found in the presacral nerve of Latarjet, whose lateral roots arise from the first to the fourth lumbar ganglia and whose middle root is a continuation of the intermesenteric plexus. In the pelvis the presacral divides into two hypogastric nerves joining the hypogastric ganglia from which postganglionic fibers pass to the lower rectum, the internal sphincter of the anus, and the pelvic viscera. The sympathetic nerves also supply the circular muscle fibers of the rectum. The effect of stimuli coming through the lumbar sympathetics is an inhibitory one upon the colon and increases the tone of the internal sphincter. The parasympathetic innervation arises from the lower sacral segments, and stimulation tends to increase the tone of the intestine, relax the sphincter, and thus initiate peristalsis.

Besides these extrinsic nerve innervations there are the intrinsic mesenteric plexuses whose main function is to make possible the conduction of nerve impulses and to correlate muscular activities; the ganglion cells in the plexuses probably prevent the intestinal muscle from contracting too hard.[1-4]

The anatomic description of the nerve supply of the colon has therefore offered an hypothesis for the origin of congenital megacolon. The

From the pediatric service of Dr. L. H. Barenberg at Morrisania City Hospital, New York, N. Y.

excess of sympathetic activity may produce an inhibitory effect, resulting in constipation, and a diminished tonus of the parasympathetic innervation of the colon which leads to inefficient relaxation of the sphincter, may have a similar effect.

Up to the year 1926 when Wade first demonstrated the value of sympathectomy,[5] numerous surgical procedures such as coloplication, colopexy, etc., were attempted, but with no satisfactory results. Nor has sympathectomy been successful in all cases. Some degree of success has been obtained in mild cases with medical therapy. The introduction of the parasympathetic activator, acetylbetamethylcholine, offers greater promise for medical therapy. Satisfactory results have already been reported by Law.[6, 7]

We have had an opportunity of following a patient with congenital megacolon, from the age of 3 months to the present time, for a continuous period of four and one-half years, during which we were able to study the effects of various drugs, medical procedures, and even surgery.

CASE REPORT

J. E., was admitted to the pediatric service of Morrisiania City Hospital for the first time on July 20, 1936, at 3 months of age. The mother stated that since the age of 2 weeks the infant had been vomiting each feeding. At 2 months of age she first noticed abdominal distention and marked constipation.

The family history was noncontributory except for a feeble-minded sister 3 years of age.

The patient had a normal spontaneous birth at the Morrisania City Hospital; birth weight was 9¼ pounds (4.2 kg.). He was discharged at 10 days of age as a normal vigorous infant weighing 8½ pounds (3.9 kg.).

Physical examination on admission to the pediatric service revealed a mildly dehydrated infant in a poor nutritional state. He weighed 9½ pounds (4.3 kg.) and had a distended and tympanitic abdomen measuring 37.5 cm. in circumference. His skin was dry, and his tongue was thick and protruding. Laboratory findings, except for a blood cholesterol of 312 mg. per cent, were essentially normal. It was the impression that this was a case of mild hypothyroidism.

Radiographic examination of the colon with the aid of a barium enema showed marked dilatation of the entire colon (Fig. 1*a*).

The infant was placed on a diet consisting of protein milk, orange juice, cereal, and banana. Thyroid extract was given for a period of three months beginning with 1/10 gr. T.I.D. and increased gradually up to 1 gr. daily. During the first two months in the hospital, although the infant was only mildly constipated, the abdomen was distended at all times. On two occasions 0.2 c.c. of pituitrin was given, but without any effect on the distention or constipation. For the next month in the hospital there was a marked increase in the degree of abdominal distention and constipation which was relieved only by frequent enemas. The infant was discharged on Nov. 5, 1936, three and one-half months after admission.

He was readmitted four days later because of vomiting, abdominal distention, and constipation. His course in the hospital during his second admission did not differ from the first. Therapy similar to that given during the first admission was used. He had no spontaneous bowel movements nor relief from distention for one and

one-half months. The infant, 8 months of age, unimproved, and in a poor nutritional state, was finally discharged to the Home for Hebrew Infants. His weight was 10 pounds 5 ounces (4.7 kg.).

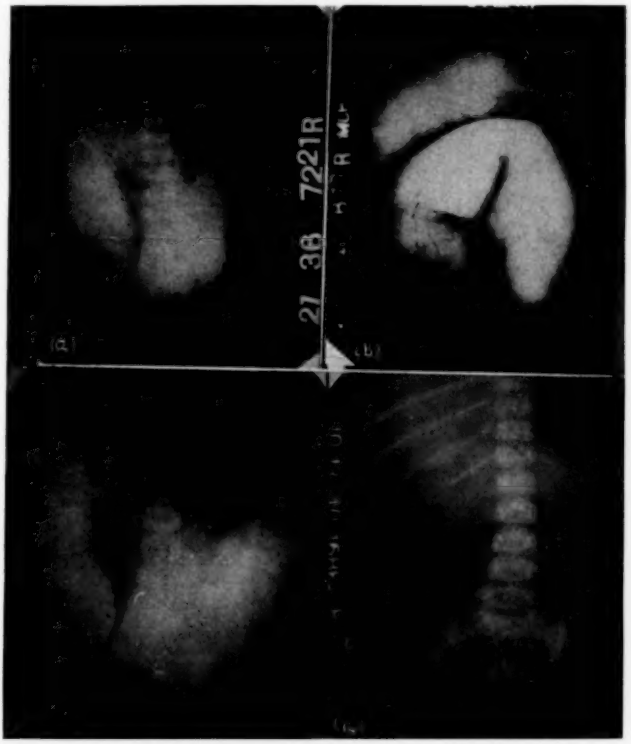

Fig. 1.—*a* and *b*, Roentgenograms taken on first and third admissions to the hospital, showing marked dilatation of the colon. *c*, Appearance of colon four months after the use of mecholyl bromide. *d*, forty-eight hours later, showing good caliber of colon and complete evacuation of the barium.

At the latter institution he was under continuous observation for two years and nine months, during which time, although his nutritional status improved to some extent, it was obvious that he was mentally and physically retarded. During this period the effects of the following medications and procedures were noted: Atropine, pituitrin, thyroid extract, syntropan, prostigmine bromide, and enemas or colonic irrigations (Table I). The only drug which we found to have any effect, although inconstant, was pituitrin. It is interesting to note that there was a period close to nineteen months when the child had an apparent remission and required only an occasional enema during this entire time. At the end of this period constipation and distention again returned and resort to pituitrin did not bring any response. Nor were the results any better with the use of prostigmine bromide or syntropan. Mineral oil brought about an alleviation of the symptoms for three and one-half months, and then the symptoms recurred. By August, 1939, the child's distention became marked, and, since we could not successfully control it, we felt that the infant should be given the benefit of a lumbar sympathectomy.

TABLE I

EFFECT OF VARIOUS FORMS OF THERAPY UPON ABDOMINAL DISTENTION AND CONSTIPATION

(July 20, 1936, to Nov. 15, 1940)

THERAPY	DURATION (DAYS)	DOSAGE	EFFECT
Thyroid	90	1/10 gr. T.I.D. to 1 gr. daily	None
Pituitrin	<1	0.2 c.c. subcutaneously	None
Enemas	50	P.R.N.	Relief
Atropine	2	1/1000 gr. A.C.	None
Pituitrin and mineral oil	18	5 min. B.I.D. 1 tbs. daily	Good bowel movement daily; abdomen soft; slight distention
None	28*		Daily bowel movement; moderate distention
Pituitrin	38	5 min. B.I.D.	Good daily bowel movement; moderate distention
Enemas	579*	Once in 2 weeks	Bowel movement every other day; abdomen distended but soft
Enemas	32	Daily	None
Pituitrin and thyroid	53	5 min. B.I.D. 1/10 gr. T.I.D.	None
Syntropan	64	15 mg. increased gradually to 130 mg. daily	At 45 mg. good effect for four days and then none
Prostigmine bromide	2	15 to 30 mg. daily	None
Pituitrin	19	5 min. B.I.D.	Good bowel movement daily; moderate distention
Mineral oil	103*	1 to 2 tbs. daily	Good
Pituitrin	16	5 min. B.I.D.	None
Enemas and colonic irrigations	25	Frequent intervals	None
Syntropan	37	45 mg. increased gradually to 150 mg. daily	None
Depropanex	7	0.3 to 0.5 c.c. I.M. every other day	None
Sympathectomy and ganglionectomy			None
Enemas and mineral oil	72	Daily; 1 to 2 oz. daily	None

*At the end of these periods abdominal distention and constipation were marked.

TABLE I—CONT'D

THERAPY	DURATION (DAYS)	DOSAGE	EFFECT
Thyroid	90	⅕ gr. T.I.D. increased gradually to 3 gr. daily	None
Pitressin	17	2 min. B.I.D. subcutaneously	None
Acetylbetamethylcholine chloride (mecholyl)	5	1 mg. subcutaneously	Marked peristalsis; bowel movements on three occasions; distention unaffected; temporary effect
Mecholyl and prostigmine methylsulfate	1	1 mg. subcutaneously ¼ mg. subcutaneously	Marked peristalsis; large bowel movement; great decrease in distention; temporary relief
Prostigmine bromide	14	7.5 mg. increased gradually to 45 mg. daily by mouth	None
Acetylbetamethylcholine bromide (mecholyl bromide) and mineral oil	120	100 mg. increased gradually to 200 mg. B.I.D. then gradually decreased to 200 mg. daily; 1 to 2 oz. daily	At least two to three good bowel movements daily; abdomen soft and not distended

In September, 1939, he was admitted to another hospital for observation and surgery. He was observed for sixty-three days during which time syntropan and depropanex (choline derivative) were given but without any therapeutic effect (Table I). After two months in this hospital a sympathectomy and ganglionectomy were performed. A portion of the right presacral nerve, about 4 cm. in length, was dissected. On the left side, the fourth lumbar ganglion and 1 to 2 cm. of the sympathetic chain were removed. The child was discharged on the twenty-fifth postoperative day, having had but two spontaneous bowel movements during that period. He had received daily enemas.

After his discharge to his home, he required daily enemas for relief of constipation and distention. His condition was unsatisfactory; his appetite was poor; and he vomited often. One month later, Jan. 9, 1940, he was admitted for the third time to the pediatric service of Morrisania City Hospital, in a poor condition. His facies was suggestive of hypothyroidism. The outstanding finding was a distended, tympanitic abdomen measuring 65 cm. in circumference with a well-healed scar in the midline extending from the symphysis up to the umbilicus. The veins over the chest and upper portion of the abdomen were dilated. The musculature over the abdomen was thin, and the colon was clearly outlined and palpable. Except for brittleness of the hair and dryness of the skin, the rest of the physical examination was negative. Weight was 30 pounds (13.6 kg.), and height was 35½ in. (89 cm.) (Fig. 2*a*).

Laboratory Findings.—R.B.C., 4,290,000; W.B.C., 17,600; 72 per cent polymorphonuclears; 28 per cent lymphocytes; hemoglobin, 80 per cent (Sahli). Microscopic examination and qualitative tests of the urine were negative. Urine creatine was 15 mg. per cent; and urine creatinine, 138 mg. per cent. Blood serology was negative; blood cholesterol was 315 mg. per cent; and glucose tolerance test was normal.

X-ray of wrists revealed carpal centers normal for the child's age. Barium enema showed marked dilatation of the rectum, sigmoid, and colon (Fig. 1*b*).

The child was placed on the house diet. During the first week no medication was given, but he required an enema every day. A three months' course of thyroid lowered the blood cholesterol to 257 mg. per cent, but there was no effect upon abdominal distention and constipation. Nor was a therapeutic effect obtained with

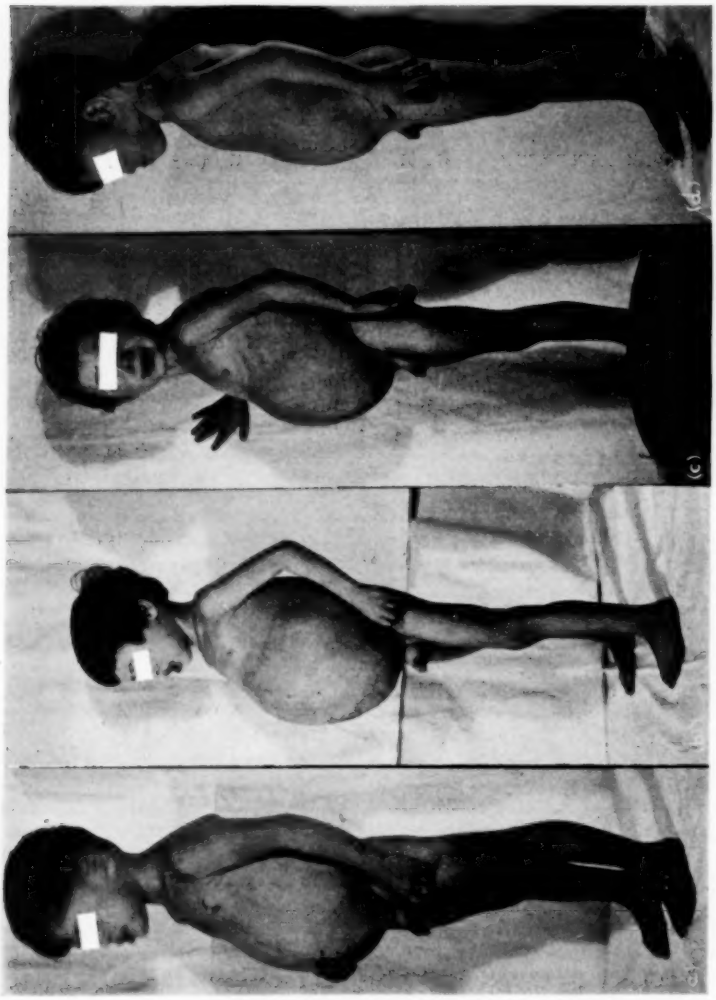

FIG. 2.—*a*, Appearance of patient upon admission to hospital on Jan. 9, 1940, at 3¾ years of age. *b*, Appearance four months after admission and before injection of mecholyl and prostigmine. *c*, One-half hour after injection of mecholyl and prostigmine. *d*, Appearance at present time.

pitressin hypodermically over a period of seventeen days. Since he was not having spontaneous bowel movements, it was necessary to give him enemas at frequent intervals. At this time acetylbetamethylcholine chloride, mecholyl, a parasympathetic stimulant which is a derivative of acetylcholine, was tried. On five different occasions, each following a period of constipation and distention of several days'

duration, 1 mg. of mecholyl was given by hypodermic. Within three to five minutes after the injection peristaltic waves were seen, and these continued for twenty minutes. There was no shock nor was the pulse rate or the general condition of the child adversely affected. On three occasions small bowel movements resulted immediately without affecting the abdominal distention. It is interesting to note that on two occasions a late effect of the drug was obtained lasting two days and five days respectively after the injection of mecholyl. The child was not constipated; the abdomen became soft; and he appeared happier. Because of the irregularity of response to mecholyl alone and because the abdominal distention became worse, a combination of 1 mg. of mecholyl and 0.25 mg. of prostigmine methylsulfate was given hypodermically. The results were dramatic. Five minutes after this injection forceful peristaltic waves appeared, each lasting one to two minutes; ten minutes later he vomited; twenty-five minutes later he had a large bowel movement lasting fifteen minutes. The abdomen at this time was about one-half the size prior to injection. In addition to the effects on the gastrointestinal tract evidence of mild shock appeared. The pulse dropped from 120 to 80 per minute; the child appeared anxious, and the skin was cold and clammy (Figs. 2*b* and *c*).

Because of the inconvenience of daily hypodermic injections of mecholyl and prostigmine and a two-week trial of prostigmine bromide by mouth which was found to be of no value, all medication was discontinued for the next two weeks. During this period constipation and abdominal distention persisted and the abdomen measured 65 cm. At this time Law's paper appeared in which he described an oral preparation, acetylbetamethylcholine bromide, for use in congenital megacolon.[6] Law's procedure was carefully followed. The child was prepared by means of one to two enemas and 2 oz. of mineral oil daily for a period of five days. Then mecholyl bromide was given in small doses before breakfast and gradually increased to 200 mg. twice a day; this was the effective dose. The results were satisfactory. The child had at least two good spontaneous bowel movements daily without any undesirable side effects. It is interesting to note that during the course of treatment, owing to the difficulty of obtaining the drug, the child did not receive mecholyl bromide for about a week without any return of abdominal distention and constipation. We were, therefore, encouraged to gradually reduce the dosage of mecholyl bromide to 200 mg. once a day. This was supplemented by mineral oil (Table I). The last roentgenographic examination of the intestinal tract by means of a barium enema reveals a definite improvement in the caliber of the colon and shows the presence of barium in the cecum where it was absent previously; an x-ray film taken forty-eight hours later shows almost complete evacuation of the barium (Figs. 1*c* and *d*). The patient at the present time is alert and active; his appetite is good; and he is gaining in weight and height. He has three good spontaneous bowel movements a day, and the circumference of the abdomen is 52.2 cm. (Fig. 2*d*).

COMMENT

The failure of sympathectomy to alleviate the symptoms in our patient may be due to an incomplete surgical procedure, for only a partial sympathectomy was done. Theoretically the best surgical results would be obtained by the removal of the presacral nerve and its lateral roots, the intermesenteric plexus, and whatever ganglionic masses are found on the inferior mesenteric artery.[3] The operation most frequently performed is the one suggested by Judd and Adson in which the second, third, and fourth lumbar ganglia are resected as well as their intervening trunks.[8] The surgical procedure carried out in our case involved

the removal of only a portion of the right presacral nerve, the fourth lumbar ganglion, and a portion of the left splanchnic. Furthermore, it is the opinion of various authors that an operation done at this early age does not yield as favorable results as does one at a later age.

Whether or not the same favorable results would have been obtained prior to operation with mecholyl bromide is purely problematical. It is quite possible that the drug supplemented the effect of the partial sympathectomy and in that manner was therapeutically effective.

We cannot definitely say that the child is cured, just as we cannot apply the term "cure" to a diabetic patient who is sugar-free while using insulin. For it must be remembered that the child was born with some derangement in the autonomic nerve supply, and as far as we know this was only, if at all, partially altered by surgery.

It must be recalled that on several occasions in the past he had a definite response to pituitrin for various periods of time, and finally he failed to respond to that drug. Therefore we cannot state with certainty that the patient will get along without mecholyl bromide or that even the present response will be permanent.

SUMMARY

A case of congenital megacolon is reported; it has been under continuous observation for a period of four and one-half years during which the effect of various medical procedures, drugs, and surgery were studied. The best results were obtained with the use of mecholyl bromide (acetylbetamethylcholine bromide) by mouth and mineral oil. The patient is completely relieved of abdominal distention and constipation, and his physical development is progressing in a normal manner.

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ANTISTREPTOLYSIN CONTENT OF THE SERA OF NORMAL INFANTS AND CHILDREN

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THE examination of the blood for content of antistreptolysin has in recent years received increasing clinical and epidemiologic application in diseases of man caused by beta hemolytic streptococci. Although the test is most commonly used as a diagnostic aid, some clinics have found it of help in prognosis, through ability to determine the probable presence of septicemia in severely ill persons several days in advance of isolation of streptococci from the blood. A low antistreptolysin titer in the presence of a severe streptococcus infection, or a pronounced decline after a previously observed high value, often coincides with blood stream invasion. In epidemiologic surveys the reaction offers the possibility of distinguishing between carriers of hemolytic streptococci and persons having actual infection in atypical, subclinical, or latent form.

The practical application of the test rests on the fact that hemolytic streptococci produce a soluble hemolysin, which is antigenic, giving rise in experimental animals to an antistreptolysin.[1] Antistreptolysin can be demonstrated in the blood of human beings after spontaneous infection, by a simple technical procedure involving neutralization of the antistreptolysin by measured quantities of standardized streptolysin. The reaction is specific, in that diseases caused by other infectious agents are not followed by an appreciable increase in antistreptolysin.[2] The formation of antistreptolysin is a characteristic of infection by all members of a given group of streptococci, for instance, Group A in diseases of man. The test does not differentiate infections with various serologic types within the group. Antistreptolysin seemingly has no important part in resistance to hemolytic streptococcus disease, although it serves as a useful index of infection. Streptococcus antitoxin and antistreptolysin are independent antibodies and do not necessarily parallel each other in their development during the course of acute streptococcus infection.[3]

Adequate knowledge of the usual level of antistreptolysin in sera of normal persons is essential to interpretation of clinical and epidemiologic results. Todd[4] considers the normal value to range between 20 and 100 units per cubic centimeter. Coburn and Pauli[5] have reported a median value of 83.3 units for normal persons; they state that 75 per cent of the people have titers of less than 100 units, 20 per cent show values from 100 to 200 units, and about 5 per cent are in excess of 200 units. Longcope[6] reports 50 units as being the usual level for adults resident in a southern city.

The studies on which this report is based were made under the auspices of the International Health Division of the Rockefeller Foundation, in cooperation with the Institute of Hygiene, Iasi, Rumania.

Practically all reports on the mean antistreptolysin titer of normal persons have dealt with adults, and singularly little information is available in respect to normal children, despite the fact that in this age group streptococcus infections are especially important and common. The best observations are those of Lippard and Johnson,[7] who report for infants aged less than 17 months, an average titer of 24 units, and for those older than 17 months, a titer of 66 units. These values were derived from the first examination of blood from sick children suffering from various streptococcal illnesses. They cannot, therefore, be considered as representing observations on strictly normal children, although it is well known that in streptococcus disease the antistreptolysin titer ordinarily does not increase until the second or third week of disease. Wilson, Wheeler, and Leask[8] have reported a correlation between antistreptolysin titer and age. This does not seem to hold for newborn infants; Coburn and Pauli[9] reported that 80 per cent of thirty-seven bloods from the umbilical cord contained more antistreptolysin than the corresponding maternal bloods.

A comprehensive study of antistreptolysin in the bloods of normal people has had as its end an effort to determine the usefulness of antistreptolysin determinations in the study of epidemics of streptococcus infection. For clinical application to the individual patient, an upward movement of the curve is of itself significant. It has developed, however, that well-defined differences exist between the mean antistreptolysin titer for children as compared with that for adults, a correlation which enters into clinical interpretation. The pertinent features of a study of normal children of ages ranging from birth to 14 years are reported.

METHODS

All persons included in the study were in good health at the time sera were obtained. These studies were made in Rumania, and sera were obtained by personal visits to the homes of the people. Conditions are rarely so favorable for obtaining samples of blood from average healthy children, especially those in the younger age groups. All were living in a normal everyday environment. None were attending outpatient departments or well-baby clinics, or were resident in institutions.

Most of the sera for determination of antistreptolysin were obtained from blood drawn by venepuncture. Samples from the newborn infants represent blood taken from the umbilical cord at the time of birth. With very young infants it was sometimes necessary to take blood from the longitudinal sinus.

The examinations were usually made within the subsequent two or three days, the sera being stored in the icebox without preservative, in tubes stoppered with paraffined corks. The technique of the antistreptolysin reaction employed in these studies has been previously described.[10]

RESULTS

The normal median level of antistreptolysin for women of childbearing age, that is, 15 to 49 years, was determined to be 62.5 units. Sera from twenty-nine mothers and their newborn infants were then examined, all samples of blood having been taken at the time of parturition. We wished to determine whether there was a regular relationship between the antistreptolysin titer of the infant and that of the mother. The actual value might conceivably be close to that of the adult, through passively transferred immunity, or it might be lowered or even absent. Unexpectedly, the antistreptolysin content of the blood of newborn infants was consistently higher than that of their mothers. The results are presented in Table I.

TABLE I

ANTISTREPTOLYSIN TITERS OF TWENTY-NINE MOTHERS AND THEIR RESPECTIVE NEWBORN INFANTS

(units per cubic centimeter)

MOTHERS	NEWBORN INFANTS
10	31.7
31.7	31.7
31.7	62.5
50	4
50	50
50	62.5
50	83.3
50	83.3
62.5	50
62.5	62.5
62.5	62.5
62.5	62.5
62.5	83.3
62.5	83.3
62.5	83.3
62.5	100
62.5	100
62.5	125
62.5	125
62.5	125
62.5	159
83.3	100
83.3	159
100	125
100	159
125	100
159	200
200	200
250	312
Median = 62.5	Median = 83.3

In almost all instances the infant's antistreptolysin titer paralleled that of the mother. With few exceptions, if the mother had a low titer, the value for the infant was also relatively low. No instance was found in which the mother had a relatively high titer and the infant a normal or low value. The median antistreptolysin titer for mothers in this series was 62.5 units, and for infants, 83.3 units.

The antistreptolysin titer of newborn infants approximated the highest value found for any subsequent age group, that of persons aged 15

to 19 years. There was a rapid and progressive decline in titer following birth, so that the mean for infants in the first three months of life was about 20 units. The low point for all age groups was reached at age 3 to 5 months when the mean titer corresponded to 10 units per cubic centimeter. Thereafter, a progressive rise was noted, reaching a maximum in adolescence. During the second six months of life, the low value of the second trimester practically doubled, to give an average value of 20 units by the time the infants had attained one year of age.

TABLE II

ANTISTREPTOLYSIN IN SERA OF HEALTHY CHILDREN, BY AGE

AGE	NO. OF CASES	OBSERVED ANTISTREPTOLYSIN VALUES, UNITS PER C.C.			
		MINIMUM	MAXIMUM	MEDIAN TITER	MEAN TITER
Newborn	29	4	312	83.3	82.65 ± 1.10
1 day- 2 mo.	16	4	50	25.0	19.11 ± 1.13
3- 5 mo.	17	2	159	10.0	10.28 ± 1.24
6-11 mo.	32	2	250	20.0	20.39 ± 1.13
1 yr.	41	4	250	40.0	34.21 ± 1.12
2 yr.	38	8	250	62.5	57.27 ± 1.09
3 yr.	18	12.5	200	62.5	62.30 ± 1.11
4 yr.	20	8	200	83.3	71.62 ± 1.10
5- 9 yr.	165	12.5	312	83.3	75.65 ± 1.03
10-14 yr.	174	16.0	833	83.3	79.86 ± 1.03
15-19 yr.	39	40.0	312	83.3	80.37 ± 1.08

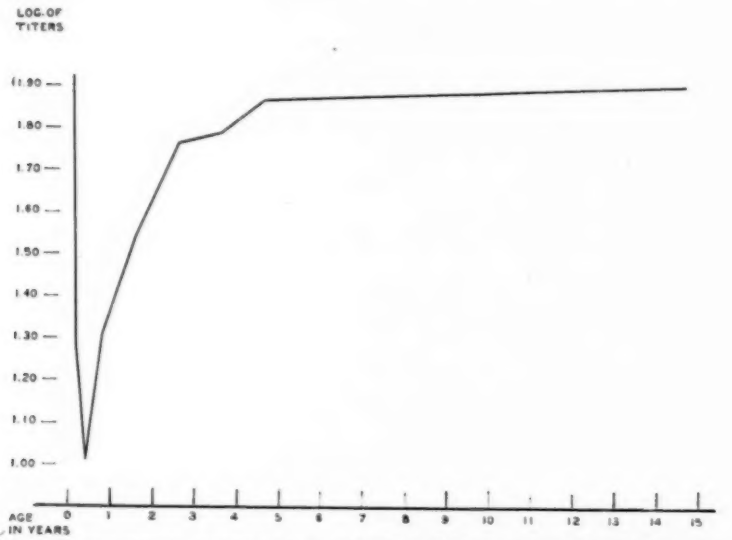

Fig. 1.—Antistreptolysin content of sera of healthy children. Mean titers by age from newborn to 14 years.

During the second year of life the antistreptolysin content again increased markedly, so that the mean value was now 34 units, and thus

continued during the third year. By the end of the fourth year, the mean titer was found to be in approximate agreement with the mean for all ages.

Titers for the age group from 5 to 9 years old showed some increase over those characteristic for children aged 4 years. Maximum values were attained during ages 10 to 19 years, when the antistreptolysin titer approximated that at birth. The progressive changes described are illustrated in Fig. 1.

SUMMARY AND CONCLUSIONS

The mean antistreptolysin titer of sera from newborn infants is higher than at any other time in life. It is greater than the average titer of the mothers of the infants. For individual infants, the value is related to that of the mother, being regularly high for infants with mothers of high titer and low when the mother's titer is low.

The high titer of the newborn infant, presumably passively acquired, declines sharply to reach a low point at ages from 3 to 6 months. Thereafter a progressive increase occurs, so that by the age of 15 years, the titer again approximates that at birth. Presumably this is due to actively acquired immunity, the result of intercurrent hemolytic streptococcus infection.

These measurements of the antistreptolysin titer of 550 healthy infants and children in Rumania give additional evidence of the time elements in infection and in natural immunity response of the human being to experience with a common type of infectious agent, beta hemolytic streptococci. It would be expected that the results would be essentially the same in the northern United States. In southern states the shape of the curve should be the same, but the values in time and degree might well be different.

The mean normal antistreptolysin content of the blood of young children differs significantly from that of adults. Correction for this difference is necessary in the interpretation of clinical and epidemiologic data.

It remains to be determined if young children with low normal antistreptolysin titers react to known infection in the same manner, in respect to degree and rapidity of antistreptolysin response, as do older children, adolescents, and adults.

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VIRUS DISEASES AND THE EYE IN CHILDHOOD

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THE purpose of this paper is merely to indicate how the eyes of children may be affected by certain diseases of virus origin. No attempt will be made to describe the viruses or their inherent characteristics or to discuss the treatment. Only the commoner diseases will be considered, because such infections as Rocky Mountain fever, psittacosis, and foot-and-mouth disease, although they may affect the eye, are seldom encountered in New York. Rabies is not included, since the ocular complications in a fatal disease are relatively unimportant. The encephalitis that sometimes follows the use of the vaccine is not attributable, of course, to the disease itself. No mention is made of such conditions as German measles, pemphigus, or sympathetic ophthalmia, because the role of virus in the production of these disorders is not yet fully established. Trachoma is included for practical purposes, although it is considered by some to be a rickettsia disease.

HERPES ZOSTER

This disease is not unknown in children. Koch[1] reported a typical case in a boy 5½ years old; and Batignani[2] found the lesion in a newborn infant whose mother had the disease at the time of parturition. Ocular complications occur in about 50 per cent of all cases. The lids are crusted by the typical eruption which usually leaves depigmented and pitted scars. The conjunctiva is rarely attacked directly, but small pustules may appear on the superior tarsal and bulbar surfaces. In the former situation they may leave deep, round scars. In severe cases extensive sloughing and necrosis may supervene. Scleritis may follow, often several months after the skin eruption has disappeared.

The cornea early loses its sensitivity. Minute subepithelial dots appear, often coalescing to form large areas of infiltration. The later stages may include keratitis profunda or keratitis disciformis, and the consequent scarring may lead to serious diminution in vision.

The iris is always inflamed if keratitis is present, and sometimes the pupil is small because of reflex miosis, even when hyperemia of the iris is absent. The iritis may be due to localized herpetic eruptions on the surface of the stroma. In such cases the inflammation is severe, glaucoma or hypotony may supervene, and the eye may be lost. Patches of depigmentation remain to indicate the sites of the eruptive lesions.

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The ocular muscles are attacked, either singly or in groups, in about 7 per cent of all cases. Complete ophthalmoplegia may be accompanied by exophthalmos. This has been ascribed by some writers to atony of the muscles, and by others to sympathetic stimulation.[3] Ptosis may be either apparent, produced by the weight of the swollen lid, or real, as a result of third nerve paralysis. Accommodation is paralyzed in some cases. As a rule, the prognosis is good, and muscular balance is restored in about six weeks.

The optic nerve is rarely involved, but if it is, a severe neuritis, followed by atrophy, may be the result.[4]

VARIOLA

In smallpox the lids do not escape the eruption, and swelling may be extreme. The conjunctiva is usually mildly inflamed from about the fifth day of the disease. Actual pustules are rare, but if present, they may extend to the cornea, with grave results. As a rule, the prognosis is favorable if the nursing is good, and the chief danger is from secondary infection.

The cornea is sometimes involved as a result of the extension of a pustule from the conjunctiva. If secondary infection occurs, the sight is usually lost. The iris may be secondarily inflamed if corneal ulcers have occurred, but a mild primary iritis is also found in about 13 to 17 per cent of all cases. It occurs on the eighth to twelfth day of the disease and is often followed by permanent patches of depigmentation in the stroma. Choroiditis has also been reported. The muscles are usually involved in the course of an orbital cellulitis, which is not uncommon. The optic nerve is rarely affected. It may be attacked directly by the virus or its toxin, or it may be secondarily involved in an orbital cellulitis.

VACCINIA

In vaccinia the lids[5] are involved either by autoinoculation or by the carelessness of the mother or nurse. The lesions are similar in appearance to vaccinia lesions elsewhere on the skin.

The conjunctiva may become infected.[6] The incubation period is three days. There is much swelling, and the eyes are "swollen shut." The preauricular gland is enlarged and tender, and there are the usual constitutional symptoms. Single or multiple ulcers appear on the palpebral or bulbar portions of the conjunctiva, and these become covered with a membrane or even with granulation tissue. Although the prognosis is good, the cornea becomes affected in about 10 per cent of the cases.

Involvement of the cornea may consist of a mild temporary marginal infiltration, or a more severe disciform keratitis.[7] An actual pustule

may form. This complication, which occurs after an incubation period of from twenty-four hours to five days, is painful and serious and may result in the loss of the eye.

The entire uveal tract may become inflamed by a metastatic process. In such a case reported by Saltini (quoted by Duke-Elder[9]), the eye had to be removed. The muscles may be involved in the course of a sinus thrombosis[10] or because of a postvaccinal encephalitis.[11] The optic nerve may be affected in degrees of varying severity. Retrobulbar neuritis was reported by von Herrenschwand,[11] and temporary blindness by Scheyhing.[12] The optic neuritis was found to be associated with retinitis by Braun.[13]

VARICELLA

In chicken pox the lids do not escape the characteristic eruption, which sometimes is succeeded by scars. The conjunctiva may be attacked by small pustules, which break down into ulcers with swollen, dark-red margins. These may extend to the cornea and produce permanent opacities. The cornea may also be attacked directly. A small vesicle may break down into an ulcer, or lead to an interstitial keratitis.[14] The deeper infiltrations usually clear up in a few months.[15]

The iris may reveal depigmented areas similar to those seen after herpes zoster. In a case reported by Hutchinson,[16] the eye was lost as a result of uveitis. The muscles may be affected in the course of the not uncommon complication of encephalitis.[17, 18] Nystagmus was observed by Lorenzo y Deal and Gastelu.[19] Optic neuritis has also been reported.[20]

MUMPS

In mumps, the vessels of the conjunctiva may be dilated, the dilatation extending to the episcleral group. There is no secretion, but there is slight edema of the bulbar portion. The symptoms subside in four or five days.[21]

The cornea sometimes becomes involved during the febrile period. The keratitis is usually unilateral and may be diffuse. It may occupy a segment of the cornea, or it may be composed of discrete patches. It is nearly always interstitial in type and subsides completely after four or five days. Rarely the formation of an ulcer may result in permanent scarring. The keratitis is sometimes associated with episcleritis.[22]

The iris may become inflamed in from three to fifteen days after the appearance of the swelling. The iritis is of varying intensity and may be accompanied by vitreous opacities. The prognosis is good.[22] Choroiditis has been reported by Laje Weskamp and Boccalandro.[23] Bonnet[22] reported the loss of two eyes following thrombosis of the central retinal vein.

The lacrimal glands may become involved. Joly (quoted by Bonnet[22]) reported this complication in 20 per cent of his cases. The swelling may be mild, or it may be painful and indurated. It subsides after several days.

The external ocular muscles, usually those innervated by the sixth and third nerves, are sometimes paralyzed, and paralysis of accommodation has also been reported. The symptoms appear during the convalescent period, usually about the third or fourth week. Recovery is the rule, but the paralysis is sometimes complete and permanent.

The optic nerve is attacked in a variety of ways. Papilledema, if present, usually disappears in from fifteen to twenty days, although one case is reported in which the nerve remained swollen for forty days.[22] In retrobulbar neuritis and neuroretinitis the prognosis is usually good, but optic atrophy has been reported by Cosserat.[24] Hemeralopia has also been observed.[22]

MEASLES

The conjunctiva is always involved in the course of measles. Four days before the onset of the rash, and two days before Koplik's spots are observed in the mouth, a mucopurulent conjunctivitis appears, accompanied by much photophobia. This usually subsides when desquamation takes place, but it may become membranous and destructive. Schachter[25] believes that there is always a turgescence of the semilunar fold (the so-called "Meyer sign") combined with a glassy appearance of the eyes one to two days before the rash, which is pathognomonic of measles. Subepithelial nodules on the conjunctiva, probably analogous to Koplik's spots, appear in the incubation period; they are yellowish and oval, and surrounded by a hyperemic ring. This finding was observed in 38 per cent of forty-six cases examined.[26]

The cornea may be affected if the conjunctivitis is sufficiently severe. The resulting ulcer may disappear, or the eye may be lost. Keratomalacia has been reported.[27] Primary iritis does not occur in measles, but a metastatic iritis may develop. Patches of choroiditis, and even widespread uveitis, have been described. Depigmented spots on the iris may be found after recovery.[28]

The muscles, both extra- and intraocular, may become paralyzed. The lesions may be unilateral or bilateral. Nystagmus, unequal or fixed pupils, and ptosis have been reported.[29] The optic nerve may be involved by retrobulbar neuritis,[30] optic neuritis, and papilledema.[29] Stellate retinitis has been reported by Stewens.[31]

HERPES SIMPLEX

In herpes simplex the lids are often the site of the familiar eruption. The conjunctiva is usually the site of slight irritative inflammation if the lesion on the lid is near the margin. This type of conjunctivitis is

never important, but a more serious pseudomembranous form may occur.

The cornea is the site of superficial vesicles which break down to form dendritic ulcers. Skin lesions may or may not be present. In Gundersen's[32] 221 cases, males and females under the age of 16 were affected equally, but above that age twice as many males as females were affected. Only one case was bilateral. Recurrences are frequent, but, on the whole, the prognosis is favorable.

Inflammation of the iris may be the result of corneal ulceration, but it may be caused by the virus or its toxins. Herpes simplex does not cause encephalitis in man, but Bergstrand[33] has reported a case of recurring facial paralysis in the course of the disease.

LYMPHOGRANULOMA INGUINALE

The lids may be inflamed and greatly swollen, but apparently this reaction is an accompaniment of the conjunctivitis.[34] The conjunctivitis is usually of the follicular type,[35] and the preauricular, submaxillary, and parotid glands may swell to such an extent as to simulate Parinaud's conjunctivitis.[36] The cornea may become the seat of ulceration and the eye may be lost.[34]

POLIOMYELITIS

In anterior poliomyeloencephalitis, any or all ocular muscles may be paralyzed. The paralyses may disappear or may become permanent.[37] Hippus and the Horner syndrome have been reported.[38] Visual agnosia may simulate real blindness.[39]

VERRUCA

When the common wart affects the lid margin, it may produce inflammation in adjacent structures.[40] The conjunctiva is usually the seat of a chronic inflammation, but acute conjunctivitis marked by photophobia is also encountered. When the cornea is affected, the keratitis is usually of the superficial punctate type. The photophobia in such cases is often intense.

MOLLUSCUM CONTAGIOSUM

The lids may be the site of single or multiple tumors varying in size from a pinhead to a cherry, covered by normal skin, but umbilicated at their apices. From these depressions, a characteristic cheesy secretion may be expressed. The conjunctivitis is usually catarrhal, but may be follicular in type. The actual tumors may be found on the bulbar conjunctiva.[41] The tumor may be situated on the cornea.[42]

TRACHOMA

The incidence of this disease in infants is high, as the children are infected very early in life by their mothers. It is the only virus disease known to show affinity for the eye alone.

The conjunctiva shows the typical follicles, which subsequently become converted into scar tissue. The cornea is attacked by pannus and the accompanying superficial ulcers, causing reduction and sometimes complete loss of vision. The lacrimal sac is often directly involved, and the lacrimal gland is sometimes invaded by extension along the excretory ducts.

INCLUSION CONJUNCTIVITIS

This virus disease is transmitted to the newborn infant from the birth canal of the mother, where, in the majority of cases, the typical inclusion bodies may be found.

The conjunctivitis appears five to nine days after birth. It may simulate catarrhal conjunctivitis of the ordinary type, or the discharge may be profuse enough to lead to a diagnosis of gonorrheal ophthalmia. In older children it is frequently follicular, and may be contracted in public swimming pools. Thygeson[43] has shown that the so-called swimming pool conjunctivitis and inclusion blenorrhea are the same disease.

SUMMARY

The common virus diseases may attack any or all parts of the eye. The ocular complications of thirteen such diseases are described.

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ACUTE APPENDICITIS AND PSEUDOAPPENDICITIS IN RHEUMATIC CHILDREN

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THE fact that an attack of rheumatic fever in children may be ushered in or accompanied by abdominal pain has been known for many years. That this abdominal pain may exhibit features which closely simulate those of acute appendicitis has also been appreciated for a long time, but it would seem that an occasional re-emphasis of this simulation is warranted, especially as some of the articles on rheumatic fever in children fail to mention the abdominal syndrome while other treatises on acute appendicitis and acute disorders of the abdomen neglect to consider rheumatic fever in the differential diagnosis.

It is doubtless true that in most instances the abdominal pain accompanying the active phase of rheumatic infection is of a mild character and, therefore, that unless questions are directed toward this point, the clinical history may not reveal its occurrence. Hence, many of the articles on rheumatic fever in children fail to mention abdominal pain as an occasional symptom. Vague abdominal aches and pains are such frequent complaints of children that those which are significant may not command the attention that they deserve.

We have been interested particularly in the children whose clinical manifestations on admission suggested acute appendicitis and whose signs and symptoms later appeared to be of rheumatic origin. It is in this group that an incorrect diagnosis frequently leads to unnecessary surgical intervention.

This report is based on a study of nineteen rheumatic children who were admitted to the Babies' Hospital with the tentative diagnosis of acute appendicitis (Table I). They were selected from a group of 262 consecutively admitted children with rheumatic fever, the majority of whom were in an active phase of the disease. In any group of this type it is natural that the manifestations of appendicitis should vary in degree; however, in every case they were of sufficient magnitude to suggest acute appendicitis to the family doctor or to the admitting physician at the hospital.

An analysis of the past history of these nineteen children revealed a record of previous rheumatic arthritis or heart disease in five, scarlet fever in one, and repeated attacks of abdominal pain in two. In one of the latter, rheumatic fever had been suspected as a possible cause of the abdominal attacks because of vague joint pains, the presence of

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TABLE

NO.	AGE	SEX	RACE	FAMILY HISTORY (RHEUMATIC)	PAST HISTORY		PRESENT ILLNESS					PHYSICAL				
					RHEUMATIC FEVER	SCARLET FEVER	UPPER RESP. INFECTION	MUSC. AND JOINT PAIN	ABD. PAIN	NAUSEA	VOMITING	TEMP.	PULSE	THROAT	JOINTS	HEART
																Operated
1	8	M	W	0	+	0	0	0	+	?	+	100.2	104	0	0	+
2	7	M	W	0	0	+	0	0	+	?	?	100.0	90	0	0	0
3	13	M	W	0	+	0	0	0	+	?	?	100.0	90	0	0	+
4	7	M	W	0	0	0	0	+	+	?	?	101.6	128	±	+	+
5	4	F	B	0	0	0	0	+	+	?	?	102.2	124	0	+	0
6	4	M	W	+	0	0	0	+	+	+	0	103.2	120	±	+	+
7	6	M	W	0	0	0	0	0	+	+	0	101.0	116	0	0	0
8	11	M	W	0	+	0	0	0	+	?	+	99.2	88	0	0	0
9	8½	M	W	+	+	+	0	0	+	+	+	99.2	106	+	0	0
10	11	M	W	0	+	0	0	0	+	+	+	100.2	120	0	0	0

I

EXAMINATION										
ABDOMEN										
TENDERNESS	MUSC. SPASM	REBOUND TENDERNESS	RECTAL TENDER.	W.B.C.	POLYS. (%)	E.S.R. (MM. PER HOUR)	OPERATION	APPENDIX	POSTOPERATIVE ARTHRITIS	FINAL DIAGNOSIS AND FOLLOW-UP
Cases										
+	+	0	+	14,280	71	4	+	Acute appendicitis	0	Acute appendicitis in a child with inactive rheumatic fever
+	0	0	+	6,700	66	—	+	Acute appendicitis (mild)	0	Acute appendicitis (very mild) in child with past history of scarlet fever; following year had similar abdominal attack with rheumatic fever
+	+	+	+	21,000	88	—	+	Acute appendicitis	0	Acute appendicitis in a child with inactive rheumatic fever
+	+	0	+	29,000	82	109 1 day postop.	+	Acute appendicitis (mild)	0	Acute appendicitis (mild) and acute rheumatic fever (mild)
+	+	?	?	21,500	88	125 1 day postop.	+	Normal	0	Acute rheumatic fever (mild) and normal appendix; following year rheumatic fever with similar abdominal attack
+	+	0	0	10,550	74	138	+	Normal	0	Acute rheumatic fever (mild) and normal appendix
+	+	?	?	20,200	80	126 2 days postop.	+	Normal	+	Acute rheumatic fever and normal appendix; three and one-half years later rheumatic fever and rheumatic heart disease (active)
+	+	0	0	11,700	81	10	+	Normal	0	Normal appendix in inactive rheumatic patient with slight bilateral hydronephrosis; six months later acute rheumatic fever
+	+	?	0	5,900	53	—	+	Normal	0	Normal appendix (except *Oxyuris*) in a child with inactive rheumatic fever
+	+	?	+	19,700	80	115 2 days postop.	+	Normal	+	Acute rheumatic fever and normal appendix (except *Oxyuris*)

TABLE 1

NO.	AGE	SEX	RACE	FAMILY HISTORY (RHEUMATIC)	PAST HISTORY		PRESENT ILLNESS					PHYSICAL				
					RHEUMATIC FEVER	SCARLET FEVER	UPPER RESP. INFECTION	MUSC. AND JOINT PAIN	ABD. PAIN	NAUSEA	VOMITING	TEMP.	PULSE	THROAT	JOINTS	HEART
Nonoperated																
11	4	F	W	0	0	0	0	0	+	+	0	102.0	124	0	0	+
12	6	F	B	0	0	0	+	+	+	?	?	103.0	120	+	0	+
13	3	F	W	0	0	0	+	0	+	0	0	103.0	118	+	0	0
14	8	F	W	0	0	0	0	0	+	+	0	103.6	120	0	0	0
15	4½	M	W	0	0	0	+	+	+	0	0	104.4	120	+	0	0
16	8½	F	W	0	0	0	+	+	+	+	+	100.8	138	+	0	0
17	10	F	W	0	0	0	0	0	+	+	0	103.0	120	±	0	0
18	11	M	W	+	0	0	0	0	+	+	+	101.6	112	+	0	0
19	5½	M	W	0	0	+	+	+	+	+	+	102.0	110	+	0	+

A question mark signifies that no mention is made of the particular symptom or sign. E.S.R.

a cardiac murmur on several occasions, and a moderately elevated erythrocyte sedimentation rate. Of the nineteen patients, ten were operated upon during the first three days after admission to the hospital. In four cases a histologic diagnosis of "acute appendicitis" was made; in two of these the appendix had been described as normal by the surgeon at the time of operation. In two of the remaining six cases in which the appendix showed no gross or microscopic evidence of inflammatory reaction, sections of *Oxyuris vermicularis* were found in the lumen of the appendix. In none of the cases did the microscopic examination of the sections of the appendix disclose findings of a nature that suggested rheumatic origin.

—CONT'D

EXAMINATION										
ABDOMEN										
TENDERNESS	MUSC. SPASM	REBOUND TENDERNESS	RECTAL TENDER.	W.B.C.	POLYS. (%)	E.S.R. (MM. PER HOUR)	OPERATION	APPENDIX	POSTOPERATIVE ARTHRITIS	FINAL DIAGNOSIS AND FOLLOW-UP
Cases										
+	+	0	0	10,000	55	122				Acute rheumatic fever; following year similar attack
+	+	+	+	13,400	77	—				Acute rheumatic fever and active rheumatic heart disease; four years later similar attack with severe abdominal pain
+	+	0	0	18,900	71	—				Acute rheumatic fever (mild); three years later similar attack with abdominal pain and vomiting, also rheumatic heart disease
+	+	+	+	18,200	91	136				Acute rheumatic fever (mild); one month later active rheumatic heart disease
+	+	?	?	32,650	65	138				Acute rheumatic fever (home against advice)
+	+	0	+	36,000	90	104				Acute rheumatic fever
+	+	0	0	21,050	89	80				Acute rheumatic fever and active rheumatic heart disease; one and one-half years later acute rheumatic fever with abdominal pain; six months later active rheumatic heart disease; died
+	+	?	?	13,800	73	106				Active rheumatic heart disease; no recurrence for next four years
+	0	0	0	16,000	70	121				Acute rheumatic fever and active rheumatic heart disease; no recurrence for next seven years

= Erythrocyte sedimentation rate (Westergren Method).

It should be mentioned that in one of the patients (Case 8), in whom a normal appendix was found at operation, surgical interference was resorted to largely because of the insistence of the parents. During each of the previous attacks of acute abdominal pain they had first been told that the boy had acute appendicitis and must be operated upon; each time, however, the abdominal signs subsided before the boy reached the operating room. A week following the extirpation of a normal appendix the boy developed gross hematuria which persisted for several days, but which was not associated with edema or hypertension; the blood chemical findings were normal. Pyelography revealed a slight degree of bilateral pyelectasis. Six months following

TABLE

ACUTE APPENDICITIS OCCURRING

NO.	AGE	SEX	RACE	FAMILY HISTORY RHEUMATIC	PAST HISTORY		PRESENT ILLNESS					PHYSICAL EXAMINATION						W.B.C.	POLYS. (%)	E.S.R. (MM. PER HOUR)
					RHEUMATIC FEVER	SCARLET FEVER	UPPER RESP. INFECTION	MUSC. AND JOINT PAIN	ABD. PAIN	NAUSEA	VOMITING	TEMP.	PULSE	THROAT	JOINTS	HEART	ABDOMEN			
20	8	M	W	0	+	0	0	+	0	0	0	103.0	104	+	+	+	0	11,000	75	117
21	11	M	B	+	+	0	+	+	+	0	+	102.8	118	0	+	+	0	11,000	86	111

operation the boy was readmitted to the hospital during an attack of frank rheumatic polyarthritis, but at this time there were no abdominal symptoms.

It is difficult to account for the subsidence of the attacks of abdominal pain following the removal of a normal appendix. A causal relationship between the pain and the mild degree of pyelectasis is not likely. The failure of the abdominal pain to recur during the attack of rheumatic arthritis six months after the appendectomy also belies its rheumatic nature. Four years have elapsed since the appendix was removed, and there has been no recurrence of abdominal pain. In fact, there have been no rheumatic symptoms since the attack of polyarthritis. He is now a vigorous, asymptomatic boy of 15 years. He still has a soft blowing systolic murmur in the apical region; otherwise the heart is normal. Further investigation of the status of the pyelectasis has not been made because of the boy's excellent physical state as well as the repeatedly negative urinary findings.

None of the ten children who were subjected to appendectomy gave a history of recent upper respiratory infection; distinct inflammation of the pharynx was present in one, and slight inflammatory reactions were seen in two others.

Of the children who were not operated upon, six showed inflammation of the throat, five of them presenting manifestations of acute upper respiratory infection. Seven of the children had pain or tenderness in one or more joints just preceding or at the time they reported to the hospital, and nine had definite evidence of rheumatic heart disease at the time of admission. Only one child developed a pericardial friction rub.

II

DURING RHEUMATIC ATTACK

DAY OF ONSET	TEMP.	ABDOMINAL SYMPTOMS: ABD. PAIN	NAUSEA	VOMITING	ABDOMINAL SIGNS: TENDERNESS	MUSC. SPASM	REBOUND TENDERNESS	RECTAL	W.B.C.	POLYS. (%)	E.S.R. (MM. PER HOUR)	OPERATION	APPENDIX	FINAL DIAGNOSIS AND FOLLOW-UP
17th	100.0	+	+	+	+	+	+	+	29,500	90	20	+	Acute appendicitis	Acute appendicitis during subsiding acute rheumatic fever; no recurrence for next two years
26th	104.2	+	+	+	+	+	+	+	10,400	88	114	+	Acute appendicitis	Acute appendicitis during acute rheumatic fever; four years later active rheumatic heart disease; died

Before proceeding with further discussion of these nineteen patients, we should mention two others (Table II) who were admitted during an acute attack of rheumatic fever. While the disease remained active, each suddenly developed acute right lower abdominal pain; in one patient this occurred on the seventeenth day, and in the other, on the twenty-seventh day after admission.

The first (Case 20), a white boy of 8 years, had been in the hospital two years before with a mild attack of rheumatic arthritis and rheumatic heart disease. Three days before admission fever and pain in the right hip had developed. On admission the rectal temperature was 103° F.; the boy looked moderately sick and complained of pain on movement of the right hip. The throat was reddened, and the cervical nodes slightly enlarged and tender. The heart was not enlarged or overactive. A double murmur at the apex suggested mitral disease. The electrocardiogram showed prolonged conduction time: the PR interval was 0.30 second. The leucocyte count was 11,000 per cubic millimeter with 75 per cent polymorphonuclears, and the erythrocyte sedimentation rate was 117 mm. in one hour. The articular symptoms subsided within a day or two without salicylate therapy, and after the fifth day the temperature and pulse remained within normal range. In the course of two weeks the PR interval had fallen to 0.26 second and the erythrocyte sedimentation rate to 30 mm. in one hour. On the seventeenth day after admission the boy became nauseated, vomited twice, and complained of acute abdominal pain. There was generalized abdominal tenderness most pronounced over the right lower quadrant. There was rebound tenderness and rectal tenderness, both experienced on the right side. The rectal temperature was normal. The leucocyte count had risen to 29,500 per cubic millimeter with 90 per cent polymorphonuclears; the erythrocyte sedimentation rate was 20 mm. in one hour. Before the results of the blood examination were known, the attack of abdominal pain was thought to be due to a mild rheumatic exacerbation. However, the high leucocyte count, the low erythrocyte sedimentation rate, the absence of fever, the absence of pains elsewhere, and the definite signs in the right lower quadrant of the abdomen strongly suggested acute appendicitis. At operation a long appendix

was found kinked around the velum from the ileum. There was no regional adenopathy. The pathologic diagnosis was "acute appendicitis and acute fibrinopurulent peritonitis." The boy had an uneventful postoperative course. For over two years he was in a cardiac convalescent home. He still shows signs of mitral disease but has had no recrudescences of rheumatism.

The second (Case 21), a negro boy of 11 years, had been in the hospital at 9½ years of age for six weeks with mild chorea and rheumatic heart disease. On several occasions after his discharge he complained of pain in his elbows and wrists. Three weeks before admission he had abdominal pain associated with chills and vomiting. A few days later he developed a head cold, suffered from abdominal pain, and vomited. A week before admission he complained of pain in the right knee and both hips. On admission he seemed moderately sick. The rectal temperature was 102.8° F.; the pulse rate, 118; and the respiratory rate, 28. He showed occasional slight choreiform movements. The left knee was slightly swollen and tender, but the other joints were normal. There was a slight postnasal discharge in the throat; nothing abnormal could be detected on examination of the heart. A diagnosis of acute rheumatic fever and chorea was made. The leucocyte count was 11,000 per cubic millimeter with 86 per cent polymorphonuclears. The erythrocyte sedimentation rate was 111 mm. in one hour. The electrocardiogram showed a slight prolongation of conduction time with a PR interval of 0.20 second. About ten days after admission a soft, blowing systolic murmur was detected over the apex, and this grew more pronounced. For twelve days the boy received salicylates. Arthropathy and fever subsided promptly. A few days after the administration of salicylates was stopped the temperature again rose to 101° F., and he complained of pain in the right foot, right hand, and neck. Salicylates were again given. The erythrocyte sedimentation rate remained high, 114 mm. in one hour. Two days following the resumption of salicylate therapy abdominal pain developed suddenly, chiefly in the umbilical region, and the child vomited. There was pronounced generalized abdominal tenderness and rigidity, both more marked on the right, as well as rebound and rectal tenderness on the right. The temperature was 104.2° F. The leucocyte count was 10,400 per cubic millimeter with 88 per cent polymorphonuclears. At first the inclination was to dismiss the abdominal signs as a manifestation of rheumatic fever. The joint pains of two days before and the continued high erythrocyte sedimentation rate were ample evidence that the rheumatic infection was still in an active state. However, after a short period of observation it was decided that further delay was not warranted and a laparotomy was performed. A small amount of pus was found about the cecum. The appendix was reddish purple, about three times the normal size, and showed evidence of perforation. Microscopic examination disclosed marked inflammatory changes but no lesions characteristic of rheumatic disease. The postoperative course was uneventful, but on discharge twenty-six days after operation the rheumatic process was still active, judging by the erythrocyte sedimentation rate which was still at 120 mm. in one hour. During the ensuing years he continued to have frequent upper respiratory infections through the winter months and occasional muscle and joint pains, rarely cardiac pain and epistaxis; signs of mitral disease persisted. At 15 years of age he was admitted to the Presbyterian Hospital with active rheumatic heart disease showing signs of double mitral disease and aortic insufficiency. This episode proved rapidly fatal.

Every one of these nineteen children presented a difficult diagnostic problem. All had acute abdominal pain, in the majority of cases most pronounced in the right lower quadrant. Nausea and vomiting were no more frequent in the children who had acute appendicitis than in

those who did not. All had abdominal tenderness, and all but two had muscular spasm. Rebound tenderness and rectal tenderness did not differentiate the two conditions. It must be conceded that some of the children whose abdominal signs were variable did not present as distinct a picture of appendicitis as did the others. Then, too, the presence of an upper respiratory infection or of muscle and joint pains called attention to the possibility of a rheumatic or other cause of the abdominal manifestations and often dictated a period of observation.

COMMENT

As has been stated before, many of the treatises on rheumatic fever do not include abdominal pain as one of the not unusual complaints during the active phase of this disease, especially at the onset of an attack. Several writers, however, have emphasized the frequency of abdominal pain in rheumatic subjects. Ash,[1] in her study of 445 rheumatic children, observed abdominal pain in fifty-six (13.2 per cent); thirteen of these had an accompanying pericardial friction rub. Coburn,[2] in a series of 162 cases of rheumatic fever, noted acute abdominal pain in thirty-two patients, who had no evidence of enlargement of the liver or cardiac insufficiency; the pain frequently occurred at the onset of a recrudescence of the disease. Swift and McEwen[3] called attention to the rather characteristic abdominal pain that often occurs in patients with rheumatic fever and, especially in children, is frequently the presenting symptom. They emphasized that such patients are often thought to have some acute abdominal surgical disorder, acute appendicitis being most frequently suspected.

Wolffe and Brim[4] found that a large percentage of children with rheumatic heart disease exhibit a group of frequently unrecognized gastrointestinal symptoms as the only manifestations of an active rheumatic phase. Hedley,[5] in speaking of the recognition of rheumatic fever, mentioned the abdominal distress which at times is severe enough to be mistaken for appendicitis. On the other hand, Findlay[6] stated that he had never observed an example of rheumatic infection in which he could unhesitatingly incriminate the abdomen as the seat of this disease.

In his comprehensive book, "Appendicitis and Other Diseases of the Vermiform Appendix," Kelly[7] recalled that the etiological relation between appendicitis and rheumatism was a matter of frequent comment by older writers, especially in the period from 1840 to 1860. In 1893 Grant[8] reported a case of "rheumatic perityphilitis" in a girl of 12 years who had had pain and a "sense of uneasiness" in her feet two days before the onset of severe abdominal pain which was referred particularly to the ileocecal region. There was tenderness and muscular spasm most pronounced below McBurney's point. Surgical interference was postponed, and four days after the onset of abdominal pain

the right shoulder, elbow, and both wrist joints became swollen and painful. As the arthritic symptoms became more pronounced, the abdominal symptoms lessened.

Since these early references there have been numerous case reports,[4, 9] of attacks of rheumatic fever in which the onset with acute abdominal pain strongly suggested appendicitis; in many instances the children were operated upon.

Giraldi[10] suggested that the abdominal symptoms of acute rheumatism may be divided into three groups: (1) Digestive group in which there is vague epigastric pain sometimes associated with nausea, vomiting, and diarrhea during an attack of rheumatic fever (the possibility of these symptoms being due to other causes such as enlarged liver, pericarditis, arthritis of the hip joint, or even salicylate medication must be borne in mind); (2) pseudoappendicular group which presents symptoms and signs of acute appendicitis; (3) peritoneal group which shows signs of a diffuse peritonitis.

Guptill,[11] in a review of 160 cases of acute rheumatic fever, encountered eight patients in whom a syndrome simulating acute appendicitis was present. In four cases exploration and appendectomy were performed, but in each case the appendix was found to be normal. The remaining four cases were held under observation as the evidence for the diagnosis of acute appendicitis was not convincing. As in our series two of his patients developed acute appendicitis during an attack of acute rheumatic fever. He emphasized in the differential diagnosis of the abdominal manifestations of acute rheumatism from acute appendicitis that in rheumatic fever there are (1) a lower incidence of vomiting, (2) a lack of spasm in the presence of diffuse and marked abdominal tenderness, and (3) a normal Schilling hemogram.

In our experience vomiting was mentioned as being present in only seven of the nineteen cases, but spasm of the abdominal muscles was noted in all but two instances. The number of our patients in whom a Schilling differential count was done is too small to justify conclusions. All seven patients in whom Schilling counts were made showed shifts to the left; one had mild acute appendicitis with no evidence of rheumatic activity, and six had varying degrees of rheumatic activity. Rogatz[12] found that both the Schilling count and the erythrocyte sedimentation rate were influenced by the rheumatic infection and that, of the two, the erythrocyte sedimentation rate was the more sensitive.

Mills,[13] in a study of the filamented-nonfilamented cell count (a modification of the Arneth and Schilling methods) in acute appendicitis, came to the conclusion that its most useful application consisted in determining prognosis, an increasing nonfilamented cell count being regarded as an unfavorable sign.

It would seem, therefore, that in both rheumatic fever and appendicitis the Schilling hemogram shows an increase in the number of im-

mature polymorphonuclear leucocytes and is therefore of no aid in differential diagnosis.

The leucocyte and differential counts in our group of cases did not prove of aid in differentiating between acute appendicitis and the abdominal syndrome of rheumatic fever (Table I).

The erythrocyte sedimentation rate, on the other hand, proved to be of distinct value. Lesser and Goldberger[14] were among the first to emphasize the value of the erythrocyte sedimentation test in the problem of differentiating cases of acute appendicitis from those showing pseudoappendical symptoms of rheumatic fever. In their study of a large series of patients with acute appendicitis as contrasted with other conditions simulating appendicitis they found that, despite a high leucocyte count in the cases in which definite acute appendicitis was demonstrated at the operating table, the erythrocyte sedimentation rate was normal. On the other hand in all other acute abdominal disorders the erythrocyte sedimentation rate was consistently accelerated. This abnormal rate was found also in all extra-abdominal conditions simulating acute abdominal disease. A number of other investigators[15] have confirmed the finding of a normal erythrocyte sedimentation rate in acute appendicitis. If perforation occurs, the erythrocyte sedimentation rate may rise rapidly to 80 mm. or over in one hour.

It is generally agreed that the erythrocyte sedimentation rate usually parallels the activity of the rheumatic process.[16] At times the leucocyte count will reach normal levels while the erythrocyte sedimentation rate is still elevated, and the reverse may also occur. In rare instances both the leucocyte count and the erythrocyte sedimentation rate may be normal even though there are clinical signs that the rheumatic process is still active. No satisfactory explanation for this unusual happening has been offered. Generally speaking, the erythrocyte sedimentation rate is regarded as one of the most helpful and reliable tests for the determination of rheumatic activity, and it usually remains accelerated for several weeks after clinical "cure" has taken place. Many conditions besides active rheumatism may increase the erythrocyte sedimentation rate, but during the early stages of acute rheumatic fever the values tend to be high, as a rule over 100 mm. in one hour, whereas in uncomplicated acute tonsillitis or nasopharyngitis lower values (40 to 60 mm.) are usually encountered.

As shown in Table I the children who had acute appendicitis and inactive rheumatic fever had erythrocyte sedimentation rates within the normal range. Some of the children were admitted to the hospital prior to the time when erythrocyte sedimentation rates were measured. All the children who showed signs of rheumatic activity had, with one exception, erythrocyte sedimentation rates over 100 mm. in one hour. Unfortunately the erythrocyte sedimentation rate was determined preoperatively in only three instances, but in the four cases in which the

erythrocyte sedimentation rate was measured after operation the tests were all done within a day or two after operation and all showed values over 100 mm. in one hour; values of this order could not be explained by the operative procedure alone. All of these children had clinical signs of rheumatic activity.

Two children developed abdominal signs after the onset of their acute rheumatic attack (Table II); the erythrocyte sedimentation rate determination was distinctly helpful in one case. In Case 20 the rheumatic attack was mild, and signs of rheumatic activity had practically subsided when the acute abdominal attack set in on the seventeenth day after admission. In this instance the high leucocyte count (29,500), the high polymorphonuclear percentage (90), the normal erythrocyte sedimentation rate (20 mm. in one hour), and the low-grade fever (100° F. by rectum), associated with abdominal symptoms and signs that strongly suggested acute appendicitis, gave added weight to this diagnosis. On the other hand, in Case 21 in which acute abdominal signs developed on the twenty-sixth day after admission clinical signs of rheumatic activity were still present and the erythrocyte sedimentation rate remained high. In this instance the persistent, pronounced abdominal signs, uninfluenced to any appreciable degree by salicylate therapy, convinced those in attendance that laparotomy was indicated. The finding at operation of an acutely inflamed appendix justified this reasoning.

It is not within the province of this paper to mention the various pathologic conditions that may simulate appendicitis. However, a brief reference to the well-known fact that abdominal pain is not an unusual concomitant of a throat infection would seem to be warranted. Brennemann[17] called attention to the fact that the abdominal pain often is the outstanding complaint in these cases. He warned against discounting or excluding the diagnosis of acute appendicitis because of the presence of a throat infection. He was convinced that many cases of appendicitis in children occur as a complication of or a sequel to a throat infection. This point must also be weighed in the examination of a rheumatic child, since acute rheumatic attacks are often preceded by upper respiratory infections. As has been mentioned before, in this series only six of the nineteen children gave a history of preceding colds or sore throats.

Nonspecific mesenteric lymphadenitis must be considered in children who come to the physician with pain in the right lower quadrant of the abdomen. In the great majority of these cases the preoperative diagnosis is acute appendicitis, and there is no reliable method of ruling out this diagnostic possibility except by laparotomy.[18] Cave[19] was of the opinion that in mesenteric lymphadenitis the pain is colicky, that pain and tenderness are more generalized than in acute appendicitis, and that rigidity is a variable feature. Furthermore, in many of his

cases of acute appendicitis the lymph nodes were enlarged. Sobel and Stetten[20] found that a fairly large percentage of cases of nonspecific mesenteric lymphadenitis showed evidence of previous infection of the appendix.

The nature of the lesions that cause the abdominal symptoms in rheumatic fever is still largely a matter of speculation. In the large percentage of patients who have but mild symptoms no laparotomy is done and inspection of the peritoneal cavity is not obtained. It is surmised that rheumatic involvement of the abdominal muscles, intra-abdominal lymphadenitis, or pain referred from the pericardium, pleura, diaphragm, or spine may be the cause of the pain.

In only one of our patients (Case 12) was a pericardial friction rub heard. This was during the first few days of the rheumatic attack when, in addition to the abdominal pain, the patient also complained of pains in several joints. However, the failure to detect a friction rub in any of the other cases does not exclude the possibility of pericarditis having been present and having been responsible for pain referred to the abdomen.

There is still a difference of opinion as to the frequency of involvement of the peritoneum in rheumatic fever. Glanzmann[21] believed that in contrast to other serous membranes it is seldom involved. Poinso and Monges,[9m] on the other hand, concluded from the number of reports of the onset of rheumatic fever that the peritoneum is no longer "le gros insouciant," as Laségue termed it.

A number of reports of "rheumatic peritonitis" may be found in the literature.[22] Wood and Eliason[9h] recounted an instance in a 13-year-old girl who had distinct heart disease and signs of peritoneal irritation. Laparotomy yielded an abundance of clear peritoneal fluid together with evidence of acute serositis and subserositis of the peritoneum, the cause of which was not apparent. The cultures were sterile. No suppurative focus was found in the abdomen. Nine days after operation she died of acute pericarditis.

Friedberg and Gross[23] described cases in which the diagnosis of abdominal rheumatism had been made and which at autopsy revealed a widespread periarteritis nodosa associated with rheumatic heart disease. From their study they concluded that "at least in some of the cases of rheumatic fever the gastrointestinal or abdominal symptoms have a definite basis in the pathological alterations of periarteritis nodosa."

Coburn [91] reported two patients who had exploratory laparotomies during rheumatic attacks. One had edema of the abdominal wall and peritoneum, subserous hemorrhage in the appendix, and marked hemorrhagic necrosis of the prevesical fat; the other showed hemorrhages into the appendix which were thought to be associated with active rheumatic disease.

Martin and Ellenberg's[9] case had no free fluid in the peritoneal cavity, but the appendix was abnormal. It showed areas of hyaline or fibrinoid degeneration of the serosa and muscular layers, as well as hemorrhage and lymphatic hyperplasia of the mucosa; no polynucleosis was seen.

None of the other cases reported in the literature revealed pathologic findings in the peritoneum or in the appendix characteristic of the rheumatic process. The same holds true for the six cases in this series in which the clinical diagnosis of acute appendicitis was confirmed by the pathologist.

In only three of the ten children who were subjected to laparotomy were a few enlarged mesenteric lymph nodes found, i.e., in two who had acute appendicitis and in one whose appendix was normal.

CONCLUSIONS

The conclusions that may be drawn from a review of cases of rheumatic pseudoappendicitis and of true acute appendicitis in rheumatic subjects, both in the literature and in our own series, are the following:

From the abdominal symptoms and signs per se the two conditions may be indistinguishable.

Pseudoappendicitis occurs almost invariably at the onset of a rheumatic attack, and the abdominal signs may be the first manifestation to appear. The abdominal pains may be diffuse in the beginning but frequently become localized in the right lower quadrant. They diminish and tend to disappear in the course of two to six days, and, as this occurs, joint pains may appear. In other instances, the abdominal and joint pains set in at approximately the same time, suggesting the diagnosis of rheumatic fever.

Symptoms and signs indicative of acute appendicitis occurring later in the course of an acute attack of rheumatic fever are more likely to be due to acute appendicitis than to pseudoappendicitis of rheumatic origin.

In acute appendicitis the erythrocyte sedimentation rate is normal unless perforation has occurred, whereas in pseudoappendicitis of rheumatic origin the rate is high. This is a useful diagnostic aid, provided one bears in mind the rare instances of acute appendicitis occurring during an acute rheumatic episode.

Although there have been a few reports of "rheumatic appendicitis," the histologic findings in cases of acute appendicitis occurring during an acute rheumatic attack are not specific.

It may be contended that often the rheumatic nature of the abdominal pains may be disputed. If other rheumatic manifestations are present, the evidence is more convincing. However, as long as there is no specific test for rheumatic fever, the diagnosis of this disease is not conclusive. In not a few instances the diagnosis is made in retrospect after weeks or months of observation.

Finally it should be borne in mind that, if after a short period of observation there is a reasonable doubt as to the existence of acute appendicitis, laparotomy should be done. Should the condition prove rheumatic in nature, no great harm is done by the operation, whereas procrastination in a case of acute appendicitis may result in death of the patient.

SUMMARY

Of nineteen rheumatic children admitted to the hospital with the tentative diagnosis of acute appendicitis, ten were subjected to laparotomy. Acute appendicitis was found in four (of minimal degree in two). In a fifth patient a normal appendix (except for *Oxyuris*) was removed, and no satisfactory explanation of the abdominal signs was found.

The remaining fourteen cases were considered to be instances of rheumatic pseudoappendicitis.

Of the nineteen children, five gave a history of a previous rheumatic episode and seven had muscle or joint pains at the time of or just before admission.

The abdominal symptoms and signs in themselves were not sufficient in many instances to differentiate between rheumatic pseudoappendicitis and acute appendicitis.

The erythrocyte sedimentation rate should prove of distinct aid in differential diagnosis.

Two additional children developed acute appendicitis, one in the middle of and the other toward the end of an acute attack of rheumatic fever.

The abnormal appendices revealed no pathologic findings that were characteristic of rheumatic disease.

CASE REPORTS

Operated Cases:

CASE 7.—Frank Z., a white boy, aged 6 years, was admitted complaining of abdominal pain. The family history was irrelevant except that a sister had died at 4 years of age of "acute appendicitis." His past history was unimportant except for frequent colds.

He awakened three nights before admission with abdominal pain chiefly in the umbilical region. The pain persisted and was associated with nausea but no vomiting. His temperature had not been taken. There had been no recent upper respiratory infection.

The boy seemed acutely ill. The rectal temperature was 101° F.; the pulse rate, 116; and the respiratory rate, 24. He kept his legs drawn up and appeared to have considerable abdominal pain. There was right-sided abdominal tenderness most pronounced in the right lower quadrant and associated with muscular spasm. The throat, heart, and extremities were normal.

The white blood cell count on admission was 20,200 per cubic millimeter, of which polymorphonuclears made up 80 per cent and lymphocytes 20 per cent.

An appendectomy was done on the day of admission. The appendix appeared normal. There were one or two enlarged mesenteric lymph nodes but no free fluid. On microscopic examination the appendix was normal.

Two days after operation the right knee became slightly swollen, red, and tender, and the erythrocyte sedimentation rate was 126 mm. in one hour. The pain subsided only to recur again followed by pain in the right shoulder and wrist. During this time a systolic murmur was detected. This murmur persisted.

At 9½ years of age he was readmitted with rheumatic polyarthritis and signs of mitral and aortic insufficiency.

CASE 10.—Henry T., a white boy of 11 years, was admitted complaining of abdominal pain and vomiting. The family history was irrelevant. At 9 years of age he had been in another hospital for a month with rheumatic arthritis and carditis and a year later was subjected to tonsillectomy. There had been no rheumatic recrudescences.

Forty-eight hours before admission he complained of malaise and of feeling chilly. Then nausea and repeated vomiting set in, followed by abdominal pain. A laxative was given. The vomiting continued, and the abdominal pain became worse. There were no associated joint pains and no recent upper respiratory infection.

The boy did not appear very ill. The rectal temperature was 100.2° F.; the pulse rate, 120; and the respiratory rate, 24. The throat was clear. The heart was overactive and enlarged to the left. A moderately loud blowing systolic murmur was heard over the precordium, loudest at the apex and transmitted to the axilla and base; also a soft diastolic murmur at the apex. Over McBurney's point there was definite tenderness and rebound tenderness, slight muscular spasm, as well as hyperesthesia of the skin over the whole right lower quadrant. High on the right, rectal tenderness was elicited.

The white blood cell count on admission was 19,700 per cubic millimeter, of which polymorphonuclears made up 80 per cent and lymphocytes 20 per cent.

The general impression was that this was acute appendicitis in a boy with chronic rheumatic heart disease.

Appendectomy was performed on the day of admission. The appendix appeared normal and on microscopic examination showed no inflammatory changes. It did contain several sections of *Oxyuris*.

Two days after operation he complained of pain in the right knee and left ankle, and the following day there was, in addition, slight swelling of these joints. The erythrocyte sedimentation rate was 115 mm. in one hour. His temperature which ranged between 102 and 104° F. during this time receded to normal as soon as salicylates were given.

Nonoperated Cases:

CASE 16.—Harriet H., a white girl, aged 8½ years, was admitted because of abdominal pain and vomiting of forty-eight hours' duration. Her family history was irrelevant. She had always been in good health until she had an attack of scarlet fever six months before; since then she had complained of occasional slight pains in her arms and legs. Two weeks before admission she developed a slight head cold associated with fever. Six days before she developed an urticarial rash after eating strawberries, and two days before admission she vomited and complained of abdominal pain. Vomiting had recurred several times, and the abdominal pain had become localized in the right lower quadrant.

The girl appeared only moderately sick. The rectal temperature was 100.8° F.; the pulse rate, 138; and the respiratory rate, 26. The throat was somewhat reddened, and the tonsils large and red. The heart and lungs were normal. The abdomen was definitely tender over McBurney's point, but there was no rebound tenderness and muscular spasm was only slight. There was slight rectal tenderness on the right side.

The white blood cell count on admission was 36,000 per cubic millimeter, of which polymorphonuclears made up 90 per cent. The erythrocyte sedimentation rate was 104 mm. in one hour.

The history of occasional muscle and joint pains and of a recent upper respiratory infection, together with a high leucocyte count and high erythrocyte sedimentation rate, suggested that the abdominal symptoms and signs might be interpreted on a rheumatic basis and indicated further observation.

Salicylates were given for the first three weeks. The abdominal signs subsided promptly. The fever, however, persisted for seven days. On the thirteenth day the patient complained of pain in the lower spine, about two weeks later of pain in the right and then the left ankle.

The roentgenogram of the heart and the electrocardiogram (except for slight right preponderance) were normal. The heart remained normal throughout her stay. The erythrocyte sedimentation rate slowly fell to normal in the course of the five weeks she was in the hospital.

Since discharge she has had occasional pains in the knees but no acute recrudescence.

CASE 17.—Betty E., a white girl of 10 years, was admitted because of fever and abdominal pain. Her family and past histories were irrelevant. Two days before admission she complained of generalized aches and abdominal cramps. There was nausea but no vomiting. The fever was high. She was given a laxative, but the abdominal pain persisted and finally localized in the right lower quadrant. Her physician made a diagnosis of acute appendicitis and sent her to the hospital.

The girl appeared apprehensive and moderately prostrated on admission. The rectal temperature was 103° F.; the pulse rate, 120; and the respiratory rate, 24. The tonsils and posterior pharynx were slightly reddened, and the anterior cervical lymph nodes were somewhat tender. The heart and lungs were normal. The abdomen was not distended. There was muscle spasm and tenderness in the right lower quadrant on deep palpation but no rebound tenderness. The rectal examination was negative.

The white blood cell count on admission was 21,000 per cubic millimeter, of which polymorphonuclears made up 89 per cent. The erythrocyte sedimentation rate was 80 mm. in one hour.

The presence of a throat infection together with only slight abdominal tenderness and spasm and negative rectal examination seemed to justify further observation.

Seven hours after admission she awoke, complained of generalized abdominal pain, and vomited. The following day the temperature rose to 104° F., and she had pain in the right ankle, but there were no objective signs. Salicylates were administered, and the temperature remained normal after the tenth day. The erythrocyte sedimentation rate, however, rose to 132 mm. in one hour during the first four weeks in the hospital and then gradually receded; also the conduction time was prolonged (PR interval = 0.27 second), and on percussion the heart was found to be enlarged; this was substantiated by roentgenogram. Also on auscultation a diastolic murmur was heard over the upper sternum; this was interpreted as due to an early aortic insufficiency. The systolic blood pressure was 120 systolic and 60 diastolic. There was no capillary pulsation.

After seven weeks' stay in the hospital she was discharged to a cardiac convalescent home.

At the age of 11½ years she was readmitted because of vomiting, sore throat, fever, and pains in the left shoulder and abdomen (similar to the previous attack).

The anterior cervical lymph nodes were enlarged and tender, and she had evidence of an active rheumatic carditis with signs of aortic insufficiency. Again

she showed prolonged conduction time (PR interval = 0.22 second) and a high erythrocyte sedimentation rate (129 mm. in one hour). She was discharged in an inactive state at the end of nine weeks.

At 12 years of age she was admitted to Presbyterian Hospital in a state of extreme cardiac insufficiency and died on the day of admission.

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THE URINARY EXCRETION OF THIAMIN IN NORMAL CHILDREN

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THERE are several methods now available for rapidly and accurately determining the vitamin B_1 content of body fluids. This can be of inestimable importance in studying the vitamin B_1 physiology of the normal organism and in diagnosing vitamin B_1 deficiency states even before they become apparent to the clinician. However, the results from different laboratories where urinary thiamin determinations have been done are at considerable variance. This disagreement may be explained by differences in method and in some instances by inadequacies or incompletely controlled experimental conditions. Figures given by the various observers for urinary thiamin excretion in normal adults and a few figures for children will be found in Table I.

TABLE I

VITAMIN B_1 EXCRETION IN URINE OF NORMAL ADULTS

METHOD	AUTHOR	RANGE IN MICROGRAMS*	MEAN IN MICROGRAMS*
Bradycardia	Harris and Leong[1]	36-105	60
Rat growth	Knott[2]	90-624 (children)	
Fermentation	Schultz, Light, and Frey[3]		497.7 (adults); 333 (children)
p-amino-acetophenone	You and Yang[4]	28-170 (diet not stated)	
p-amino-acetophenone	Melnick, Field and Robinson[5]	90-350 (males) 61-146 (females)	198 93
Thiochrome	Karrer and Kubli[6]		100
Thiochrome	Westenbrink and Goudsmit[7]	70-330 (males) 60-240 (females)	230 120
Thiochrome	Schroeder[8]	100-400	150
Thiochrome	von Ritsert[9]	110-520	
Thiochrome	Hills[10]	50-170	100
Thiochrome	Sciclounoff[11]	30-200	
Thiochrome	Sciclounoff[12]	30-over 200	
Thiochrome	Jolliffe et al.[13]	319-676	497
Thiochrome	Magyar[14]	43-507	86
Thiochrome	Widenbauer, Huhn, and Ellinger[15]	0.7-192	
Thiochrome	Borson[16]	75-290	166
Thiochrome	Wang and Yudkin[17]	137-233	
Thiochrome	Najjar and Holt[24]	94-208 (children) 60-342 (adults)	158 (children) 146 (adults)

*The varied units of expression have been translated into micrograms; 3 μg of crystalline thiamin chloride corresponds to one international unit.[18]

Since few figures have been published on the thiamin excretion of children, we felt that it would be of value to study a group of normal children under controlled conditions. We decided that daily determina-

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tions for at least a month would give a better understanding of vitamin B_1 physiology than isolated analyses on a large number of children.

Therefore, we studied for at least a month twenty-two children, twenty girls and two boys, who ranged in age from 4 to 10 years. They were selected with consideration for anticipated cooperation and availability for hospitalization. They were "normal" subjects, as adduced by history and physical and laboratory examinations. Anorexia, fatigue, constipation, and calf-muscle tenderness were not present at any time, nor were there any abnormal cardiac or neurologic findings. Progressive weight gains were noted in all children during the month preceding and the month of the study.

These children were kept on one of the hospital wards, and hospital life was made to approximate home environment as much as possible. They went to school, played, exercised, and rested. Considerable freedom was permitted the children in the regular hospital diet which was adequate in all the essential elements of nutrition. For at least one month the daily dietary intake of each child was carefully checked and computed in terms of total calories, grams of carbohydrate, fat, and protein, and micrograms of thiamin (estimated from the tables of Williams and Spies[19]). The average daily diet was found to contain 2,159 calories, of which 85 Gm. were protein, 237 Gm. carbohydrate, and 96 Gm. fat. The daily vitamin B_1 intake averaged 990 μg (330 I.U.) of thiamin, giving a ratio of approximately 45 μg (15 I.U.) per 100 calories.

During this period, daily twenty-four-hour determinations of the urinary excretion of thiamin were made. We used the thiochrome method of Jansen,[20] as modified by Hennessy and Cerecedo[21] and further improved by Hennessy in personal communication with us. In brief, the urine is adsorbed on permutit, and the thiamin is eluted with potassium chloride, and then oxidized to thiochrome by potassium ferricyanide; the intensity of the fluorescence in ultraviolet light is measured with the aid of a photoelectric cell and galvanometer.

The average thiamin output was 268 μg, with a range from 92 to 602 μg. Table II gives the range of each child's intake and output. At the end of the study, each child was given a 5-mg. oral test dose with the noonday meal. The percentages of excretion of this test dose varied widely and are also given in Table II.

It has been demonstrated that the thiamin excreted in the urine is dependent upon: (1) the amount ingested; (2) the amount absorbed in the intestines; (3) the metabolism of the organism; (4) the quantity of urine and, possibly, the kidney threshold.

In these normal children, the average amount of thiamin excreted was 27.2 per cent of the amount ingested. This is in agreement with the work of Light and co-workers[22] on rats in excretion equilibrium. They found 25 to 35 per cent excreted in the urine, 20 to 30 per cent in the feces, and the remainder unaccounted for. This ratio does not continue

TABLE II

NAME	AGE (YR.)	WEIGHT (LB.)	B_1 INTAKE (μG)			B_1 OUTPUT (μG)			PERCENTAGE OF EXCRETION OF 5-MG. ORAL TEST DOSE
			HIGH	LOW	AVERAGE	HIGH	LOW	AVERAGE	
S. B.	7	56¼	1182	813	981	305	113	239	8.8
B. B.	8	58½	1680	591	1020	403	169	279	3.7
Q. C.	7	57	1347	801	1005	401	170	273	11.4
D. C.	7	60	1482	663	990	489	192	301	8.0
R. C.	10	74	1650	663	1047	540	216	364	6.7
E. D.	5	50	1242	696	942	472	183	266	10.3
P. F.	9	74	1233	522	930	347	92	200	9.0
S. G.	9	86	1701	678	1059	420	123	300	7.1
E. H.	10	83	1386	801	1014	548	171	289	18.3
J. K.	8	61	1119	825	972	353	164	254	11.5
J. L.	10	69	1188	858	1020	427	140	245	8.8
L. M.	8	58	1224	816	990	488	115	209	8.7
C. M.	9	68	1224	720	969	482	247	376	9.8
M. M.	8	57	1128	825	999	299	143	214	8.6
M. O'D.	10	68	1251	636	1002	302	124	204	7.0
J. O.	7	60	1065	429	858	472	179	305	
A. P.	9	73½	1368	777	1017	420	129	263	7.0
N. S.	9	64	1227	633	990	338	167	231	5.0
T. T.	4	36	1179	660	999	275	133	193	6.3
R. T.	6	51	1329	765	990	407	213	279	3.3
R. V.	9	76	1410	777	1017	603	231	359	15.5
J. D.	7	60	1344	828	1017	366	116	253	8.9

to be true when large test doses are given. Here, the factor of the amount absorbed in the intestines in different persons is of great importance. Schultz and his co-workers[23] have shown that high doses are incompletely absorbed. We believe this explains the varied results obtained with our test doses. The indications are that smaller test doses will yield more information when used to detect latent vitamin B_1 deficiency.

The optimal thiamin intake is that amount which will best contribute to maximum health. This level is difficult to ascertain at present in the human being. For children in this age and weight group, 45 μg (15 I.U.) per 100 calories, or about 990 μg (330 I.U.) daily, seem adequate to provide for excellent health and give a constant 25 per cent urinary excretion.

The amount of urine will influence proportionately the thiamin output, if the other factors are completely controlled. Since these factors vary, we have found that recording results as micrograms per 100 c.c. of urine is not as helpful as recording the total number of micrograms of thiamin excreted in twenty-four hours.

In most instances, determinations were done on the first specimen voided in the morning, in addition to the total twenty-four-hour determinations. No constant relationship was found between the two, and it was not possible to predict the total twenty-four-hour vitamin B_1 output from the amount in the morning urine.

It should be emphasized that a single day's determination of thiamin excretion may be misleading. Occasionally marked daily variations are present. The average of several days' specimens or composite samples will give results of greater accuracy.

SUMMARY

The urinary excretion of thiamin in normal children ranged between 92 and 602 μg per day and averaged 268 μg.

For children in this age and weight group, an intake of 45 μg (15 I.U.) of thiamin per 100 calories, or 990 μg (330 I.U.) daily, seemed adequate to provide for excellent health.

The average amount of thiamin excreted was 27.2 per cent of the amount ingested.

The morning urine thiamin determinations do not furnish a constant ratio to the total twenty-four-hour output.

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FAVORABLE END RESULTS IN ICTERUS GRAVIS NEONATORUM

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THE neurological sequelae of icterus gravis neonatorum have been described in previous papers.[1, 2] These sequelae result from nuclear jaundice and intracranial hemorrhage. Klingman and Carlson[3] found that, among 675 children with neuromuscular dysfunction characterized by mental retardation, spasticity, ataxia, and choreo-athetosis, forty-five had passed through a severe neonatal jaundice averaging ten weeks in duration. It is probable that these children demonstrated the end results of nuclear jaundice or cerebral hemorrhage following icterus gravis. Lightwood and Hawksley[4] pointed out that icterus gravis has a high incidence of sequelae particularly from damage to the brain. Elsewhere they[5] remarked that nuclear jaundice is a cause of residual extrapyramidal symptoms—spasticity, athetosis, and mental deficiency—at a later age period. In still another paper[6] they stated that spontaneous intracranial hemorrhage may be even more common than nuclear jaundice, the former having been found post mortem in six of eighteen fatal cases of icterus gravis. Fitz Gerald, Greenfield, and Kounine,[7] reporting three cases of neuromuscular dysfunction following icterus gravis, remarked that the nervous sequelae of kernicterus may be found more frequently than a perusal of the literature might lead one to imagine. Strong and Marks,[8] describing icterus gravis, stated that in some, who apparently recover, mental deficiency and spastic diplegia may occur at a later date as a result of intracranial hemorrhage or nuclear jaundice. Macklin[9] stated that a child saved from icterus gravis is in danger of developing cerebral lesions owing to injury to the nervous system during the disease. The literature contains many cases[10] of idiocy, blindness, choreo-athetosis, convulsions, opisthotonos, and extrapyramidal spasticity following nuclear jaundice from icterus gravis.

It is only natural that a realization of these appalling neurological sequelae should have cast doubts upon the long-run advantages of successful immediate therapy in severe cases of icterus gravis of the newborn infant. It is everywhere admitted that modern methods of treatment can save infants with this disease who formerly would have succumbed. The question arises in many instances whether we are doing these infants and their parents a real service by saving their lives. The knowledge that an infant cured of icterus gravis not infrequently becomes a spastic idiot with choreo-athetosis and opisthotonos can hardly be expected to be a stimulus to active therapy. With a fuller realiza-

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tion of the extent and frequency of the neurological sequelae of this disease comes a greater cynicism as to the practical value of treatment during the neonatal period. To combat this increasingly pessimistic point of view it would seem to be of value to report two cases of icterus gravis saved by transfusions who are normal and in excellent condition six and one-half and seventeen months, respectively, after the onset of the disease.

CASE 1.—The patient, a female infant, weighing 8 pounds 2 ounces, was born on Feb. 21, 1939. The significant facts in the family history are as follows. The mother's first child, a boy, was born in 1924 and is healthy. The second child, a boy, was born in 1926 and died during the first week of life with severe jaundice. In 1927, during the eighth month of her third pregnancy, the mother was delivered of a dead baby. No further data on this birth are available. In 1929 the mother gave birth to a girl baby who was desperately ill for one month with severe jaundice. This child, when 10½ years old, was quite healthy and normal mentally. Her weight was 78 pounds; height, 58 inches. Physical examination was negative. In 1932 the mother was delivered of a premature, dead infant. No further data are available on this birth.

The present pregnancy and delivery were uneventful. The Wassermann reactions of the mother and father were negative. The baby cried immediately after birth. There were no signs of asphyxia. It was noticed in the delivery room that the baby had jaundice.

The patient was first seen by me when she was 6 hours old. The skin and sclerae were markedly icteric. The smooth, firm edge of the spleen was palpable 2 cm. below the costal margin. The liver extended 4 cm. below the costal margin. Physical examination was otherwise essentially negative. The blood count (Table I) revealed marked erythroblastemia and definite anemia. A transfusion of 80 c.c. of citrated blood was given nine hours after birth.

On February 22 the jaundice had deepened. The baby was apathetic, and appeared very sick. On February 23 the jaundice was even more pronounced. The general condition was worse. The urine was dark amber; the stools, light brown. The spleen had grown larger and was now palpated 5 cm. below the costal margin. The Moro reflex was present. A second transfusion of 80 c.c. of citrated blood was given. On February 24, the patient's general condition was improved. The jaundice remained the same. Edema of the vulva appeared. On February 26, the vulval edema began to recede. Although the intensity of the jaundice remained the same, the baby's condition showed a marked improvement. She took her formula more vigorously. By March 1 the vulval edema had disappeared. The icterus was less pronounced. The liver and spleen were smaller, the latter extending only 2 cm. below the costal margin. The patient's general condition was good. She was more alert and took her feedings readily. The jaundice slowly faded, and the patient was discharged on March 18, weighing 8 pounds 11 ounces. Her course was completely afebrile. At no time were there any twitchings or convulsions.

The patient was examined frequently during her first year. She developed normally and was healthy. She held up her head at 6 weeks and was able to sit up at 7 months. The first tooth appeared at 6 months, and she had five teeth at 11 months. At that time she weighed 20 pounds 8 ounces. The spleen, which was still palpable when she was 4½ months old, was no longer felt when she was 6 months old.

The patient was admitted to the hospital on March 27, 1940, at the age of 13 months and discharged on April 14. One day previous to admission she had begun to cough. Three hours prior to her entrance to the hospital she had had a severe generalized convulsion lasting fifteen minutes with cyanosis and loss of consciousness.

TABLE I

LABORATORY DATA: BLOOD COUNTS

DATE	FEB. 21	FEB. 22	FEB. 24	FEB. 25	FEB. 27	MARCH 1	MARCH 3	MARCH 6	MARCH 16
Erythrocytes per cu. mm.	2,900,000	3,500,000	4,000,000	4,100,000	4,050,000	2,900,000	3,700,000	4,060,000	3,700,000
Hemoglobin (Sahli) (Gm. per 100 c.c.)	13.2 (86%)	12.3 (80%)	15.4 (100%)	15.2 (98%)	14.8 (96%)	12.3 (80%)	12.6 (82%)	15.4 (100%)	12.3 (80%)
Erythroblasts per cu. mm.	31,000	15,700	300	0	0				
Leucocytes per cu. mm.	55,000	21,300	9,700	11,000	10,000				
Polymorphonuclears (%)	79	59	52	64	41				
Immature polymorphonuclears (%)	40	20	20	28	24				
Lymphocytes (%)	20	28	29	13	50				
Monocytes (%)	0	6	6	13	4				
Eosinophiles (%)	0	1	3	6	0				
Basophiles (%)	0	0	0	0	0				
Myelocytes (%)	1	6	10	4	5				

Urine: Feb. 22, positive for bile; Feb. 24, negative except for many epithelial cells.
Blood: Group 0.

The temperature was 101° F. Physical examination revealed a severely ill child with dilatation of the alae nasae. Dullness and markedly diminished breath sounds were elicited in the left posterior chest. A roentgenogram of the thorax was negative at this time. A Type III pneumococcus was obtained from the nasopharynx by the Auger method. Sulfapyridine therapy was instituted. The next day the patient's condition was worse. Crepitant râles and bronchial breathing were heard in the left posterior chest. A roentgenogram of the thorax demonstrated consolidation of the left lower lobe. A transfusion of 140 c.c. of citrated blood was given. The child was cyanotic and desperately ill for the next six days. It was necessary to keep her in an oxygen tent constantly for the first ten days of her hospital stay. Sulfapyridine therapy was continued for eleven days. During the first week the patient's temperature varied between 100.4° F. and 102° F. By April 7 her condition was much better. She continued to improve and was discharged from the hospital in good condition.

TABLE II

LABORATORY DATA: BLOOD COUNTS

	MARCH 28	MARCH 29	APRIL 2	APRIL 9
Hemoglobin (Sahli) (Gm. per 100 c.c.)	13.7 (89%)	13.6 (88%)	12.4 (81%)	10.5 (68%)
Erythrocytes per cu. mm.	4,410,000	4,510,000	4,400,000	
Erythroblasts	0	0	0	
Leucocytes per cu. mm.	15,800	13,650	12,600	
Polymorphonuclears (%)	54	58	36	
Immature polymorphonuclears (%)	32	17	14	
Lymphocytes (%)	43	39	54	
Monocytes (%)	2	3	6	
Eosinophiles (%)	0	0	2	
Basophiles (%)	0	0	2	
Myelocytes (%)	1	0	0	

Urinalyses were negative. The icteric index on April 2 was 13.2, Van den Bergh reaction was faint, direct, positive, and delayed. Blood sulfapyridine concentrations were 3.6 and 7.3 mg. per 100 c.c. The tuberculin patch test was negative.

The patient was seen at my office on Aug. 1, 1940, at the age of 17 months. She had been walking for the previous two months. Muscular coordination was excellent. She could pronounce a few simple words. Weight was 25 pounds 11 ounces; height, 33 in.; circumference of head, 19 in.; circumference of chest, 19 in.

CASE 2.—The patient, a girl infant weighing 6 pounds 3 ounces, was born on March 25, 1940. This was the mother's first pregnancy. Her blood Wassermann reaction was negative. The delivery was somewhat prolonged, and forceps were used. When the baby was less than 1 day old, jaundice was noticed. I first saw the patient on March 28. She presented the severest grade of deep icterus. The sclerae were yellow. The hard and soft palates showed marked jaundice. The smooth firm edge of the spleen was felt 3 cm. below the costal margin. The liver was palpable 3 cm. below the costal margin. Pallor of the lips and conjunctivae was apparent. The patient was weak and lethargic, and her condition was critical. The physical examination was otherwise negative. During the previous day she had had six watery, green stools. The urine left a dark brown stain on the diaper.

A transfusion of 65 c.c. of citrated blood was immediately administered. The infant was given nothing but 5 per cent glucose in Ringer's solution by mouth for twenty hours, and then small quantities of protein milk with 5 per cent dextrimaltose. The patient remained desperately ill, and the diarrhea continued. On

TABLE III

LABORATORY DATA: BLOOD COUNTS

	MARCH 28	MARCH 29	MARCH 30	MARCH 31	APRIL 2	APRIL 4	APRIL 10	APRIL 15
Erythrocytes (millions per cu. mm.)	3.0	3.8	2.6	4.1	4.0	4.15	4.25	4.7
Hemoglobin (Sahli) (Gm. per 100 c.c.)	9.9 (65%)	10.7 (70%)	11.6 (75%)	10.5 (68%)	11.6 (75%)	12.4 (81%)	11.0 (75%)	12.4 (81%)
Leucocytes per cu. mm.	5,800	5,200	7,100	5,700	6,400	7,100	5,000	9,400
Monocytes (%)	2	2	2	4	4	2	0	5
Polymorphonuclears (%)	72	52	38	40	36	22	52	68
Lymphocytes (%)	25	44	58	49	60	76	48	27
Eosinophiles (%)	1	0	2	1	0	0	0	0
Myelocytes (%)	0	2	0	4	0	0	0	0
Erythroblasts per cu. mm.	106	52	0	0	0	0	0	0
Basophiles (%)				2				

March 30 a second transfusion of 75 c.c. of citrated blood was administered. Following this there was a slow steady improvement in the patient's condition. On April 13 the infant's weight was 6 pounds 13 ounces. Edema of the vulva was noted, but receded during the next week. She left the hospital on April 16, weighing 6 pounds 7 ounces. Moderate jaundice was still present. The spleen was palpable 3 cm. below the costal margin. The patient's course had been completely afebrile.

She was admitted to the Lenox Hill Hospital on April 24, 1940, at the age of 1 month. For the previous three days the baby had had six to eight watery, green stools daily. She had been weak and listless and had taken her feedings poorly. Physical examination revealed a desperately ill infant who was apathetic and hard to arouse. The cry was weak. The tongue was dry, but otherwise there were no obvious signs of dehydration. The jaundice was somewhat greater than it had been the previous week. The spleen was hard, and its edge was felt 3 cm. below the costal margin. The liver was felt 3 cm. below the costal margin. There was some abdominal distention. Otherwise the physical examination was negative. The weight was 6 pounds 13 ounces. A transfusion of 55 c.c. of citrated blood was administered. The infant was given nothing by mouth but 5 per cent glucose in Ringer's solution for twenty-four hours, and then small quantities of protein milk with 5 per cent dextrimaltose. On April 26 a fourth transfusion of 70 c.c. of citrated blood was given. The infant's condition rapidly improved following this. The jaundice slowly receded. She was discharged on May 27, weighing 8 pounds. She was no longer icteric. The spleen was still palpable 2 cm. below the costal margins. The infant's hospital stay had been afebrile.

The patient has been examined frequently during the four and one-half months following her discharge from the hospital. She has thrived and developed normally. On August 7 her hemoglobin was 11.6 Gm. per 100 c.c. (75 per cent), Sahli. On Aug. 29, 1940, at the age of 5 months she weighed 15 pounds 9 ounces. Circumference of the head was 16.5 inches; chest circumference, 17.5 inches; length, 25 inches. The tip of the spleen was still palpable. Otherwise the physical examination was negative. Tissue turgor, muscular strength, and coordination were excellent. The infant was alert, in splendid condition, and seemed normal in every way. She was again seen on Sept. 18, 1940, when she was almost 6 months old. Weight was 17 pounds 8 ounces; length, 25¾ inches; circumference of head, 16⅝ inches; circumference of chest, 17¾ inches; hemoglobin (Sahli), 11.6 Gm. (75 per cent). The baby was beginning to sit up with slight support. She was alert, noticed objects readily, and was able to pick them up. Physical examination was completely negative. The spleen was no longer palpable, and the liver was not enlarged. The patient was last seen on Oct. 9, 1940, at the age of 6½ months. Weight was 19 pounds 7 ounces; circumference of head, 17½ inches; circumference of chest, 18 inches; length, 26¾ inches. The physical examination gave negative findings. The infant was in excellent condition. She sat erect with only slight support and could easily roll from back to stomach or vice versa. She used her hands to reach and grasp and pick up a small object on the examining table. She cooed, smiled, and laughed readily while playing. The infant seemed normal in every way.

DISCUSSION

Case 1 was a classical example of icterus gravis. Following this episode during the neonatal period, the patient thrived and was able to successfully withstand a severe attack of Type III pneumococcus lobar pneumonia at the age of 13 months. Case 2 was a somewhat less typical example of icterus gravis in that an erythroblastemia in excess of physiologic limits was not demonstrated. Cases of true icterus gravis

have, however, been reported without erythroblastemia.[11] Moreover, a blood count was not taken until the fourth day of life. The early, extraordinarily intense and prolonged jaundice, the desperate condition of the infant, the persistently enlarged liver and spleen, the hyperchromic anemia, the edema, and the response to transfusions, all occurring without any other explanatory cause, lead to the conclusion that the case was one of icterus gravis.

Zucker and I[2] have emphasized a tetralogy characteristic of the end results of nuclear jaundice or cerebral damage caused by icterus gravis. This tetralogy consists of opisthotonos, choreo-athelosis, extrapyramidal spasticity, and mental defectiveness. The two patients reported here presented none of these signs. Stigmata of a previous intracranial hemorrhage were likewise completely lacking. In fact, all who observed these infants at the ages of 6 and 17 months, respectively, were impressed by their alertness, mental fitness, and splendid physical condition.

Macklin[9] believed that the evidence indicates that icterus gravis is due to a dominant mutation and that the opportunity exists for a direct transmission of the defect to 50 per cent of the offspring of an individual so affected. Darrow,[12] on the other hand, is of the opinion that statistical analyses show that, while icterus gravis is a familial disease, it is not inherited. Knowledge about the exact diagnosis and successful treatment of icterus gravis is so recent that sufficient time has not elapsed for any considerable number of persons with proved instances of the disease to reach the reproductive period. There seems to be no reason why the two now apparently healthy patients here reported upon should not in the ordinary course of events attain normal adult life. When more infants such as these reach the age of reproduction and bear children, an opportunity will exist to test the hypothesis of the inherited nature and transmission of icterus gravis. This is for the future to decide.

CONCLUSIONS

The frequent occurrence of neurological sequelae following icterus gravis neonatorum is discussed.

Two cases of icterus gravis are reported. The infants, now 6½ and 17 months, respectively, are without neurological residua and appear normal in every way. One successfully withstood a severe attack of Type III pneumococcus lobar pneumonia at the age of 13 months.

Although the end results of icterus gravis are often appalling, active therapy during the neonatal period is of real value since an apparently normal infant may be the reward of successful treatment.

As more healthy infants cured of icterus gravis reach the reproductive period, it may be possible to directly test the hypothesis of the hereditary nature and mendelian transmission of this disease.

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SKULL FRACTURES IN CHILDREN AND THEIR SEQUELAE

A Critical Analysis of 285 Cases

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IT IS a general belief that the sequelae of skull fractures in children are less severe and less frequent, and that the prognosis is more favorable than with similar injuries in the adult. This opinion is based upon certain anatomic peculiarities of the child's skull which give protection not offered by the adult skull. These are the elasticity of the skull due to the presence of membranous bones, the adherence of the dura mater to the skull, limiting and preventing extradural hemorrhage, and the buffering action of the cartilage and fibrous tissue between the bones, which decreases the force of the blow to the brain tissue.

This study was made (1) to determine the frequency and severity of the immediate symptoms following skull fractures in children, and (2) to find out how these children get along in later life, and what complaints or findings they present years after their injury. Our study is based on 285 patients with skull fracture who were admitted to the Milwaukee Children's Hospital between 1922 and 1939. In order to avoid confusion and controversy, only proved cases of skull fractures are included in this series. In all cases, one or more of the following findings were present:

1. X-ray evidence of fracture—260 cases
2. Autopsy findings of fractures—4 cases
3. Bleeding from the ears or orifices, with signs of intracranial injury indicating basal skull fracture—21 cases

Approximately twenty-five cases which were included in the hospital diagnostic files as skull fractures might have been added to this study, but these were dropped from our list because they failed to meet the above criteria.

The records of the 285 cases were carefully studied and analyzed, and the important symptoms and findings were tabulated. With the aid of the Social Service Department of the hospital, we located 134 of the 285 patients who were residing in or near the vicinity of Milwaukee. These 134 patients were then examined at the clinics of the hospital.

AGE GROUPS

There were twenty-four patients in our group under the age of 1 year who sustained skull fractures. These fractures were the result of the child's falling out of the crib, high chair, or parent's arms.

From the Milwaukee Children's Hospital.

TABLE I

FREQUENCY OF SKULL FRACTURES AT VARIOUS AGES

AGE (YR.)	NO. OF CASES
Under 1	24
1-2	12
2-3	18
3-4	29
4-5	34
5-7	69
7-9	53
9-12	46

Between the ages of 1 and 3 years, most accidents were caused by falls due to unsteady gait. By far the largest number of cases occurred after the age of 4 years. These were chiefly the result of traffic accidents.

IMMEDIATE SYMPTOMS AND SIGNS

Shock.—Severe shock as manifested by cold clammy skin, weak and rapid pulse, subnormal temperature, and unconsciousness was present in fourteen patients, seven (50 per cent) of whom died. Death in these seven occurred rapidly and in all instances within forty-eight hours. Beekman[1] reported a large number of skull fractures in children, and showed that 74.5 per cent of the patients who died within forty-eight hours died of shock. These figures indicate that a patient sustaining a head injury and in shock has a grave prognosis and that all possible measures to combat shock should be undertaken immediately before any diagnostic or extensive examinations are made.

Unconsciousness and Stupor.—One hundred and thirty-three (46.6 per cent) of the patients were unconscious, and ninety-eight (34.3 per cent) were stuporous. It was noted that those cases associated with a long period of unconsciousness usually presented more evidence of intracranial injury. From our series of cases, it appeared that the duration of the unconsciousness was a rough index of the severity of the intracranial damage.

Vomiting.—Sixty (21 per cent) of the patients vomited after their injury. This number was considerably lower than the 63 per cent quoted by Ireland.[2]

Subjective Symptoms.—Subjective complaints were noticeably infrequent in our series of cases. These children, when they recovered from unconsciousness or stupor, rarely had complaints unless there were associated injuries or complications. About eighteen (16.3 per cent) complained of headaches, and only nine (3.2 per cent) of dizziness. Complaints of loss of hearing and tinnitus were seldom encountered, although it was noted that there were forty-five patients with associated bleeding from the ears. Our experience revealed that children were not likely to have subjective complaints of headache, dizziness, loss of hearing, tinnitus, or blurring of vision. This was

in decided contrast to our experience with adult skull fracture cases in which the patient's subjective complaints often overshadowed the objective findings.

NEUROLOGIC FINDINGS

Table II shows the various neurologic disturbances found in this series of 285 cases.

TABLE II

Facial weakness, unilateral	7
Facial paralysis, complete, unilateral	1
Hemiplegia	2
Meningitis	5
Meningismus	3
Paralysis of a lower extremity	1
Convulsions	2

LOCAL SIGNS OF INJURY

In 138 (48.4 per cent) cases, lacerations, contusions, and ecchymosis were found over the site of the fractures demonstrated by x-rays. This high correlation between the local signs of injury and underlying fracture corresponded with similar findings by Ireland.[2]

Associated Fractures.—In twenty-five cases, fractures of other bones complicated the skull fractures and necessitated a prolonged hospital stay.

OTOLOGIC FINDINGS

The importance of an early and adequate ear examination is reported by Grove,[3] Blegvad,[4] Murphy,[5] Hand,[6] and others. In our series, forty-five (15.8 per cent) cases had bleeding from one or both ears; it was impossible to determine accurately the number of these cases that were associated with the escape of cerebrospinal fluid. Thirty-one patients (10.8 per cent) were found to have a spontaneous nystagmus upon admission to the hospital, indicating a disturbance of the vestibular mechanism. Six of these forty-five patients died, a mortality of 13.3 per cent as compared with the general mortality of 5.26 per cent (see Table IV). In six patients of this group suppurative otitis media developed as a complication and was followed in three instances by meningitis and death. Gurdjian,[7] analyzing an extensive series of head injury cases, stated that where bilateral aural bleeding was present, the death rate was 67.3 per cent. Bleeding from the ear usually indicates a basal skull fracture involving the temporal bone and may be associated with other clinical evidence such as escape of cerebrospinal fluid or involvement of the seventh and eighth cranial nerves which it lodges. When blood or cerebrospinal fluid escapes from the ear, the injury must be looked upon as being equivalent to a compound fracture, as there is danger of introducing secondary infection from the auditory canal or through the upper respiratory

tract. In addition, infection may go through the lacerations of the dura and produce a meningitis. Our usual treatment of these cases has been to place sterile cotton in the outer canal wall or to cover the entire ear with a sterile mastoid dressing. As a rule, the spinal fluid drainage ceases after from four to five days. The occurrence of acute suppurative otitis media or mastoiditis must be considered as a serious complication because of the danger of meningitis. Operative intervention may be necessary early. It might be added that our cases of meningitis occurred before the advent of sulfanilamide and its related drugs. We believe that with the favorable response of other types of meningitis to these drugs, the mortality of this dreaded complication will be considerably reduced. Involvement of the venous sinuses may take place as a direct result of the fracture tearing its wall or by secondary infection. In one of our cases, autopsy demonstrated a large tear through the lateral sinus, with an extensive subdural hemorrhage.

Bleeding From the Nose and Throat.—Bleeding from the nose and throat was present in forty-one (14.4 per cent) cases. Excluding local causes for bleeding from these areas, it was usually found with fractures of the anterior or middle cranial fossa. A common complication is the extension of the fracture through the paranasal sinuses, particularly the frontal and ethmoid, thereby exposing the fractured area to the outside. Cerebrospinal rhinorrhea may be an associated finding. Two of the patients (0.7 per cent) with bleeding from the nose and throat developed meningitis and died. Gurdjian and Shawn[8] reported the incidence of skull fractures involving the paranasal sinuses as being 5 per cent. The incidence of meningitis as a complication was 0.8 per cent. It is important, however, to remember that the frontal and sphenoid sinuses in children under 7 years of age are scarcely developed, and that the incidence of this complication would, therefore, be correspondingly less frequent.

OPHTHALMOLOGIC FINDINGS

In the diagnosis of skull fractures, especially when the patient is unconscious, any help offered by an eye examination is important. The work of Blakeslee[9] has shown that the ocular findings are a most valuable indicator of the degree of brain damage and may have a great diagnostic significance. A consideration of the pupils has shown that when an extreme amount of dilatation and fixation is present, a mortality of almost 100 per cent results. Studies made by Carter[10] concur in this fact. A review of our records of the more serious cases and those in which death occurred revealed that more attention should be directed to such eye findings. In eight cases dilated pupils were found, in which, however, the reaction to light was retained. There

was, however, no mortality in these cases. Unequal pupils were found in two patients both of whom recovered. Only one patient with fixed pupils was recorded as recovered.

A most important eye sign is ecchymosis of the eyelids and subconjunctival hemorrhage. This occurred in our series in forty-seven (16.5 per cent) cases. Reviewing these cases, we found that there was an associated fracture in some part of the anterior or middle cranial fossa based on x-ray evidence in forty-two of these cases. In only five of these forty-two was there other evidence, such as local trauma to the nose or lacerations to the eyebrow or lids, to account for this ecchymosis. Therefore, in thirty-seven cases the ecchymosis was derived directly from the fracture of the skull. This indicates that the presence of an ecchymosis to the lids should immediately bring serious consideration of a fracture to the anterior and middle cranial fossae. In one case the ecchymosis was severe enough to produce a proptosis.

The presence of an abducens paralysis was noted in four (1.4 per cent) patients, all of whom recovered during their stay in the hospital. One instance of a total ophthalmoplegia of the right eye occurred; subsequently this improved.

Examination of the fundi was rarely noted on the records. One case of retinal contusion occurred, associated with some retinal hemorrhage. There was one case of severe bilateral intraocular injury, with subsequent total blindness. There was a left hemophthalmus followed subsequently by a phthisis bulbi. The right eye also had an intraocular hemorrhage. A choked disk was noted in one case. This indicates that an examination of the fundi is not particularly useful, except probably in the later stages of skull fracture cases. Kearney[11] and Cohen[12] both agree that a constant finding of slight edema, as characterized by a little blurring of the disk margin and engorgement of the retinal veins, is rather constant.

LUMBAR PUNCTURE

Forty-nine (17.2 per cent) patients had spinal punctures performed, and of these, twenty-two (7.7 per cent) showed bloody fluid from the head injury. It is interesting to note that during 1938 and 1939 there were forty-five skull fracture admissions and on only two were spinal punctures performed. There were no deaths in this latter group. In our review of the literature we still found considerable controversy as to the indication and value of this procedure in head injuries (Craig,[13] Eagleton,[14] Ireland[2]). Although this series of forty-five cases during 1938 and 1939 is too small to attempt to draw any conclusion, it does indicate a definite trend at the Milwaukee Children's Hospital to refrain from diagnostic or therapeutic spinal punctures.

THERAPY

In reviewing the management and treatment of the skull fracture cases at the Milwaukee Children's Hospital, it is obvious that the trend has been toward conservative and symptomatic treatment. Ten of our cases (3.5 per cent) had a decompression done, with one death in this group. The tendency toward avoiding operative procedures is seen in the following figures. Prior to 1933 there were 135 skull fracture admissions, eight of whom were operated upon, and there were thirteen deaths in the entire group (9.6 per cent). Between 1933 and 1939, 150 skull fracture cases were admitted, and only two required operation for depressed fractures which produced pressure symptoms. In this entire series there were only two deaths (1.33 per cent). This striking difference in the number of deaths in two almost equal groups indicates that the present-day management has resulted in a distanct lowering of the mortality. It is a rule at the hospital that all patients with craniocerebral injury, even the mildest, be put at bed rest for a period of two weeks before permitting regular activity. As pointed out by Mock,[15] surgical intervention should be reserved for the following cases:

1. Markedly depressed skull fractures, simple and compound, producing pressure symptoms
2. Cases associated with middle meningeal hemorrhage
3. Cases associated with subdural hemorrhage

SEQUELAE

As mentioned previously, the Social Service Department of the hospital was able to have 134 patients return to the clinics for examination. The time interval between the date of injury and return for examination varied considerably. No cases were included in this series, however, unless at least one year had elapsed after the head injury. The average time elapsed was 5.8 years. In our review of the literature on skull fractures in children, we found numerous references concerning the acute manifestation of head injuries, but very few references relative to late complications. The patients and their parents, on returning to the clinic, were closely questioned about the immediate and subsequent progress after dismissal from the hospital.

In most cases the information concerning immediate progress was obtained from the outpatient follow-up notes. After careful evaluation of the history and the subjective complaints offered by the patients, a detailed examination was made, with particular reference to the auditory, vestibular, and visual mechanisms. These studies offered the examiners means of obtaining objective evidence which would confirm the subjective complaints of the patient.

Headaches.—This was the most common complaint and was found in thirty-nine (29.9 per cent) of the 134 patients. In only nineteen (14 per cent) cases were the headaches of sufficient severity and frequency to cause the patient to seek medical care. In these nineteen cases no factor other than the head injury was found to account for the headaches. In most instances there was a history that the headaches were related to the physical activity of the individual and were aggravated by physical fatigue and exertion.

Dizziness.—This symptom was present in eleven (8.2 per cent) cases of this series and was considered to be of sufficient severity as to distress these patients. Three of the eleven patients showed distinct vestibular disturbance as demonstrated by the caloric tests (Kobrak method); in two patients a spontaneous nystagmus was present. Many other children had vague complaints of vertigo, but only in those patients in whom it was severe enough to interfere with the physical activities of the child, was it considered significant.

Disturbances of Hearing.—All patients in this series were carefully examined for any hearing loss. These tests included the whispered voice, tuning fork, and audiometer studies. Patients with local ear, nose, and throat disturbances which might produce a hearing loss were eliminated from this group. A significant hearing loss which could be attributed to the head injury was encountered in eleven (8.2 per cent) patients. The hearing loss in most cases involved the nerve zone regions. In four cases there was a marked drop at the 4096 pitch of the audiometer curves. Tinnitus was noted in seven (5.2 per cent) patients, in five of whom there was a distinct hearing loss.

Neurologic Sequelae.—In this series the following neurologic findings were encountered: hemiplegia, one case; facial weakness, one case; and post-traumatic epilepsy, two cases.

Retarded School Work.—Nineteen (14.1 per cent) gave a history of repeated failures in an attempt to carry on their usual schoolwork. A personal communication from the Milwaukee Public Schools indicates that the average percentage of failures in children during 1938 and 1939 varied between 5.6 and 5.8 per cent. These failures tend to show that a head injury may interfere with the intellectual development of the child. Strecker[16] states that the seriousness of a head injury in a child is determined by its occurrence at a time when the child's intellectual faculties are being developed.

Ocular Sequelae.—Examinations of the patients who returned to the clinics showed that all the cases of ocular paralyses had recovered, with the exception of the one patient who had had a total right ophthalmoplegia. This patient showed a residual ptosis three years and five months later. The patient with the severe bilateral intraocular injury, who was examined eleven years eight months later, had a left phthisis bulbi and the right eye fixed in a marked lateral position,

with a large mass of retinitis proliferans involving the disk. In one instance where there had been an ecchymosis and contusion to the orbital region and a pupil that did not react to light, a right optic atrophy was found, with a superior peripheral field defect. The pupillary reactions had recovered entirely.

MORTALITY

There were fifteen deaths in this series of 285 cases, a mortality rate of 5.26 per cent. The causes of death in these cases are outlined in Table III.

TABLE III

CAUSES OF DEATH

CAUSES	NO. OF DEATHS
Shock	7
Meningitis	5
Bronchopneumonia	1
Toxic diarrhea	1
Anesthetic death	1

We have already mentioned that seven of the deaths occurred within twenty-four hours as the result of shock, and that the remaining eight deaths were the result of secondary complications. As pointed out by Mock,[15] the deaths occurring within twenty-four hours represent a group of patients who are so severely injured that probably no line of treatment would sustain life. In order to study the relative mortality of skull fracture cases in children, a questionnaire was sent to ten children's hospitals in different sections of the United States, and the information obtained was tabulated. The mortality figures as obtained from the records of these institutions are shown in Table IV.

TABLE IV

COMPARATIVE MORTALITY RATES IN ELEVEN HOSPITALS

HOSPITAL	PERIOD OF YEARS	TOTAL NO. OF SKULL FRACTURES	NO. OF DEATHS	PERCENTAGE
A	15	74	5	6.75
B	15	215	12	5.58
C	15	62	5	8.06
D	13	79	6	7.6
E	10	29	4	13.8
F	13	57	17	29.8
G	15	302	25	8.24
H	11	13	1	7.7
I	15	38	5	13.1
J	15	311	16	5.14
K (Milwaukee Children's Hospital)	17	285	15	5.26

Eight of the eleven institutions had a mortality rate of under 8.25 per cent, and three institutions (B, J, K) admitting a total of more than 800 cases, had a mortality rate of slightly over 5 per cent. Comparison with adult skull fracture mortality figures (16.6 per cent, as

given by Mock[15]) would indicate that children have about a 50 per cent better chance for life than adults with an equal grade of skull fracture.

CONCLUSIONS

In a study of this type, we realize that it is not possible to cover completely all phases of this vast subject. We have attempted to make a critical analysis of the records and to evaluate the importance of the immediate symptoms and signs that follow skull fractures in children. A follow-up study and examination were made of a large number of these cases in order to determine the incidence and severity of sequelae.

The importance of shock can be seen in the fact that it was present in fourteen cases, resulting in seven deaths within forty-eight hours. Unconsciousness was present in 46.6 per cent of the cases, and the duration appeared to be directly related to the degree of intracranial damage. Subjective symptoms such as headaches and dizziness were seldom encountered. The frequent occurrence of bleeding from the ears, spontaneous nystagmus, and ecchymosis of the eyelids suggests the importance of early and thorough otologic and ophthalmologic examinations. Sequelae resulting from the head injury, although not as common as those found in adults, are sufficiently frequent and warrant consideration because of their possible effect upon the development of the child. An important factor in preventing sequelae and complications appears to be proper management of the child at the time of the injury. An adequate period of bed rest, combined with conservative measures, has given us our most favorable results.

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OSTEODYSTROPHIA DISSEMINATA

Report of a Case

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PATHOLOGIC conditions of bone in which widespread rarefaction with cyst formation occurs show metabolic differences on which differential classifications may be based. Three distinct groups are now recognized namely, (1) hyperparathyroidism, (2) renal rickets, and (3) osteodystrophia disseminata. These three conditions possess an identical histopathology of bone which is characterized by decalcification followed by cystic degeneration with giant cell invasion as seen in osteitis fibrosa cystica. The features differentiating the three groups may be tabulated as in Table I.

In 1931 Braid[1] first recognized the third group as an entity and described a case following icterus gravis neonatorum in a male of 4 years. McCune and Bruch,[2] Albright and his co-workers,[3] and Adams, Coupere, and Jerome[4] have added about twenty cases to date. This condition, to which Albright gave the name osteodystrophia disseminata, is characterized by multiple areas of osteitis fibrosa cystica which are limited almost entirely to one side of the body. The disease occurs more frequently in females and begins in the first few years of life. Sexual precocity has been present in all cases seen in females, and excessively pigmented areas of the skin on the side more involved have been found in practically every patient.

A patient with history and physical findings similar to the cases previously reported has been followed for ten years at the Children's Hospital of Pittsburgh and is herein described:

J. M., a 3-year-old white male, was first admitted to the Children's Hospital in July, 1930, because of a right-sided limp. Physical examination showed a shortening of the right leg with some muscular atrophy. Roentgenograms of the right femur revealed an old united fracture below the trochanters, a marked bowing of the shaft, and a cystic appearance of the shaft and neck. A biopsy of bone taken during an osteotomy and curettage showed typical osteitis fibrosa cystica. The postoperative course was uneventful, and the patient was discharged fifteen days later to be followed in the outpatient department. In August, 1931, eleven months later, he was readmitted because of a fracture of the right femur which healed rapidly. The patient was again admitted on Nov. 18, 1931, for postoperative examination. In February, 1932, he was readmitted for an excision of a bone cyst from the upper shaft of the femur. The excised specimen again showed an osteitis fibrosa cystica. After a lapse of six years, he was seen on Oct. 5, 1938. At this time physical examination showed a hard tumor mass in the right maxilla and a marked deformity

From the Pathological Laboratories, University of Pittsburgh and Children's Hospital.

TABLE I

CONDITION	PARA-THYROID	BLOOD N.P.N.	BLOOD CA	DISTRIBUTION OF FIBROCYSTIC CHANGES	SERUM PHOS-PHATASE	URINARY EXCRETION OF CA	INTESTINAL EXCRETION OF CA	SKIN PIG-MENTATION	SEXUAL PRECOCITY
Hyperpara-thyroidism	Adenoma	Normal	High	Generalized	High	High	Normal	Absent	Absent
Renal rickets	Hyper-trophy	High	Normal	Generalized	High	Normal or low	High	Absent	Absent
Osteodystrophia disseminata	?	Normal	Normal	Regional or uni-lateral	High	Normal or low	High	Present	Present in females

of the right lower leg in addition to the changes originally noted in the thigh. Roentgenograms showed a large cyst of the maxilla and a dense opacity in the region of the right maxillary sinus. An osteotomy of the right tibia was performed with the hope of correcting the deformity, but little improvement was accomplished. A biopsy of the tibia was diagnosed osteitis fibrosa cystica. Blood calcium and phosphorus, taken at that time, were 9.4 mg. and 5.4 mg. per 100 c.c. of blood, respectively. In January, 1939, the patient was seen because of a greenstick fracture of the shaft of the femur.

During the following months he was examined in the outpatient department for check-up and treatment. Blood chemistry determinations at different dates gave the following results: Sept. 2, 1940, 12.5 mg. calcium per 100 c.c.; September 15, 28 mg. N.P.N. and 93 mg. sugar; September 23, 9.8 mg. calcium and 4.2 mg. phosphorus per 100 c.c.

TABLE II

BLOOD CHEMISTRY

DATE	N.P.N. (MG.)	SUGAR	CALCIUM (MG.)	PHOSPHORUS (MG.)	SERUM PHOSPHATASE (ARMSTRONG UNITS)	SERUM ALBUMIN (GM.)	SERUM GLOBULIN (GM).
1/ 2/40			12.2	3.9	67		
1/ 3/40	33						
1/ 4/40			10	3.6	62		
1/ 8/40		Tolerance normal					
1/11/40						4.5	2.4

TABLE III

CALCIUM BALANCE

DATE	OUTPUT			CALCIUM INTAKE (MG.)
	URINE (MG.)	STOOL (MG.)	TOTAL (MG.)	
1/12/40	83	No elimination	83	114
1/13/40	102	No elimination	102	114
1/14/40	137	185	322	114
1/15/40	87	374	461	114
1/16/40	83	No elimination	83	114
1/17/40	126	146	272	114
1/18/40	91	192	283	114
1/19/40	110	464	574	114
Total	819	1361	2180	912

Physical examination on readmission, Feb. 2, 1940, showed a 13-year-old white male with marked bony deformities. The skin was warm and dry, had a normal texture, and was darkly pigmented. The pigmentation was probably normal because the child was of Spanish extraction. However, there were two irregularly outlined, more deeply pigmented areas above the left buttock and over the sacrum. The face was deformed by a large, hard, painless tumor mass in the right maxilla which caused a broadening and lengthening of the right side of the face. The lesion encroached upon the right nasal passage and had also forced the teeth in the right upper jaw out of alignment. The remainder of the face and head was normal. The chest, both upper extremities, and the left lower extremity were normal. The right leg was markedly deformed. The femur showed severe anterior and lateral bowing in the varus position. The tibia was curved in the valgus position, causing a marked shortening of the leg and giving it an "S" shape. The knee was stiff because of

bony malposition and could not be flexed beyond an angle of 150°. The hip joint could be partially flexed, but there was some limitation to lateral motion. Examination of the genitalia showed a marked development for a male of 13 years. The right testicle was approximately of normal size, but the left was about twice the normal size. The penis was of average size. The left breast was enlarged and appeared to be about the size usually found in a girl of this age. Roentgenograms of the entire skeletal system showed an extensive destructive process resembling osteitis fibrosa cystica in the upper third and head and neck of the right femur. The shaft of the femur, tibia, and a portion of the right ilium were all involved, but less severely. The bones of the right foot also showed a considerable degree of rarefaction. The bones of the right arm and hand, left leg, and left arm showed no changes, but there were cystic lesions in the middle phalanges of the left fourth and fifth fingers. The tumor mass in the right maxilla has already been described.

Blood chemistry and calcium balance studies are shown in Tables II and III respectively. Seventy-five International units or six Oesting units of androgenic substance were present in a twenty-four-hour urine specimen. The basal metabolic rate and hematological studies showed nothing abnormal.

DISCUSSION

Our case bears a striking resemblance to many of the reported cases of osteodystrophia disseminata in the unilateral distribution of the bony lesions and the pigmentation. Definite evidence of sexual precocity was not present although the left testicle was considerably larger than normal. The urinary androgen was within normal range. However, sexual hyperfunction was absent in all five previously reported male cases in the literature. Evidence of kidney disease, as in all other cases, was lacking.

During the calcium balance studies, the urinary excretion of calcium with a high calcium diet was so low in several twenty-four-hour periods that an accurate determination of the quantity excreted was not possible. The physiologic basis for the excretion of the excess calcium through the intestinal tract is not clear and awaits further experimental studies on calcium excretion under various conditions. The hypocalcinuria and normal blood calcium suggest the absence of parathyroid involvement. No attempt was made to determine surgically whether the parathyroids were abnormal.

There was no jaundice or other evidence of disturbed liver metabolism, such as was found by Braid.[5] This author postulated liver dysfunction as a major factor in the development of the osseous pathology in his two cases. Albright, in a review of the reported cases, suggested that the regional or unilateral distribution of the bone lesions and skin pigmentation is due to a neurologic or embryologic rather than a metabolic disturbance. To add weight to this theory, Albright referred to the mental deficiency in one case. A further point, which has not been noted in the literature and which may be of etiological significance, is the preponderance of the bony lesions on the right side of every patient except one. In this case, Goldhamer[6] noted the association of left-sided lesions with left-handedness. This fact may indicate a pos-

sible relationship between the osseous lesions and the central nervous system, or the possibility that slight differences in metabolic activity of one side of the body determine the primary site of the lesion.

CONCLUSIONS

A case of osteodystrophia disseminata observed for ten years is reported.

Possible etiological factors are reviewed.

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ARTERIOLOSCLEROSIS, HYPERTENSION, AND CEREBRAL ATROPHY IN AN INFANT

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THE occurrence of arteriolosclerosis in childhood is being recorded with increasing frequency. Guild, Kindell, and Gibson[1] recently collected a group of twenty-two such cases, the youngest of which was a child 3½ years old. The patient we report is of interest, first, because of his extreme youth (20 months of age) and, second, because of the associated advanced degree of cerebral cortical atrophy.

CASE 1.—C. H., a white, male infant aged 20 months, was admitted to the Children's Hospital of Philadelphia on Dec. 2, 1937. The family history was irrelevant. He was a full-term infant of normal birth, weighing 7 pounds. At 1 month of age he developed a skin eruption which was said to be "measles" and which lasted for two weeks. There were no other difficulties in the neonatal period. His development was normal; he sat up at 6 months, walked at 11 months, and talked in short sentences at 17 months. His first teeth erupted at 7 months. His parents had always considered him a bright, intelligent, and active child. His dietary history was a normal one, except that he did not receive optimal amounts of vitamin D.

At 2 months of age he was circumcised. Other than having a sporadic "cold," his health was good until the onset of the illness for which he was admitted to the hospital.

At 18 months of age he developed an ulceration of the meatal orifice of the penis, which, according to the description given by the mother, resembled the lesion produced by ammoniacal diaper irritation. For several weeks he voided with difficulty, and the urethral orifice had to be probed on many occasions to start urination. During this period the child's general health was good.

One week prior to admission to the hospital he developed an upper respiratory tract infection, accompanied by fever, restlessness, and rapid breathing. The presence of pneumonia was then suspected. During this period fluids were refused, and dehydration and ketosis ensued. At this time his urine was said to contain albumin and white blood cells, and his blood urea nitrogen was reported to be 92 mg. per cent.

On admission to the Children's Hospital he was stuporous and dehydrated. His tissues were flabby, and his general nutritional state seemed below par. Even though he was 20 months old, his anterior fontanel was still open. While there was apparent bossing of his skull bones and a slight increase in head circumference, there were no other clinical or x-ray evidences to suggest rickets or renal hyperparathyroidism. The fontanel was not tense, and signs of increased intracranial pressure were lacking.

A slight nasopharyngitis was present. Dentition was normal.

Externally, the eyes were negative. However, the ophthalmologist reported definite constriction of the retinal arteries.

The lungs were normal.

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The heart was enlarged both to the right and left, the left border being about 2 cm., outside the nipple line. A soft, systolic apical murmur was heard, and the aortic second sound was louder than is usual. The blood pressures in the arms varied between 145/80 mm. Hg and 175/110 mm. Hg and were the same or slightly higher in the legs. The peripheral blood vessels were not tortuous or sclerotic to palpation. (No vascular calcification was noted in the x-ray.) There was no evidence of cardiac insufficiency.

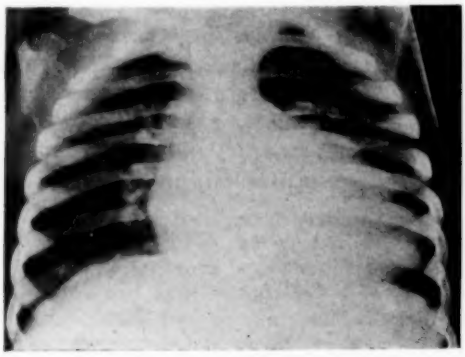

Fig. 1.—Teleroentgenogram showing cardiac enlargement.

The liver was slightly enlarged with its edge 3 cm. below the costal border. The spleen and kidneys could not be palpated. No abnormal abdominal masses could be detected.

There still remained some irritation at the meatal orifice of the penis.

Neurologic examination was negative.

The urine examined on admission contained a moderate amount of albumin, an occasional white blood cell, and one-plus acetone. (There was still some meatal irritation, and dehydration was present when this urine sample was collected.) Urine specimens examined on the next five days were free of albumin but contained four to five white blood cells per high power field (uncentrifuged). At this time a meatotomy was performed, following which the meatal infection cleared. With the subsidence of this meatal infection the subsequent twenty daily urinalyses were entirely normal. (Pus cells had entirely disappeared.) Urine obtained by cystoscopic drainage of both ureters was normal, and all urine cultures (made after the clearing of the meatal infection) from bladder and ureters were sterile. An Addis count done about one month after hospital entry was normal. (Amount, 115 c.c. of urine; specific gravity, 1.031; acid reaction; albumin, 7.2 mg.; R.B.C., 920,000; W.B.C., 115,000; no casts.) A later Addis count done following an acute upper respiratory tract infection showed a slight abnormality (R.B.C., 2.8 million and casts, 70,000). The intravenous phenolsulphonephthalein test showed normal kidney function (thirty minutes' excretion was 35 per cent, with the total one and three-quarter hours' excretion being 100 per cent). There were several blood urea nitrogen estimations, all within normal limits, the highest single value being 16.8 mg. per cent. The blood phosphorus was 5 mg. per cent, and the blood calcium, 9.4 mg. per cent. The blood carbon dioxide combining power determinations on two occasions were 64 and 65 vol. per cent. The urinary tract, according to the urologist, was normal. However, the roentgenograms made following retrograde pyelography showed some enlargement of the right renal pelvis, but without any blunting of the kidney calyces. This

pelvic enlargement seemed to have narrowed rather sharply at its junction with the ureter. In view of the absence of obstruction to the retrograde flow of the contrast medium into the renal pelvis, it is felt that a severe degree of stricture was not present. This narrowing at the ureteropelvic junction could have been produced either by a stricture of the ureter or some aberrant blood vessel crossing at this junction.

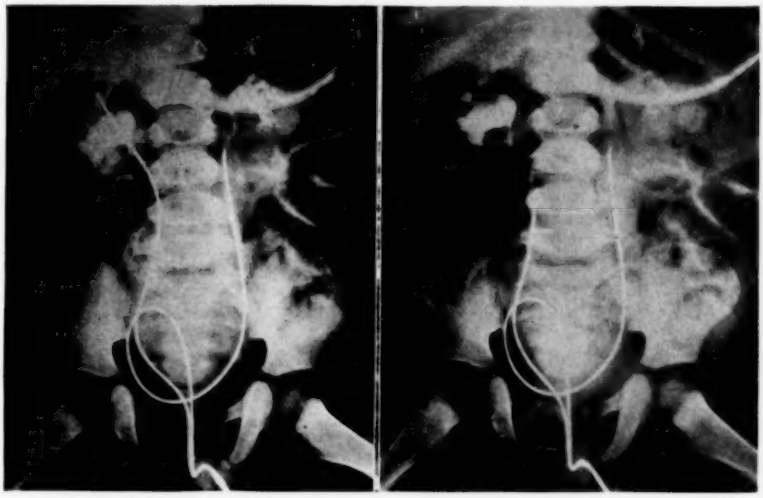

Fig. 2. Fig. 3.

Figs. 2 and 3.—Retrograde pyelograms showing normal left renal pelvis and moderate dilatation of the right renal pelvis. Constriction of the ureteropelvic junction (right) is visible in Fig. 3.

The admission blood count showed red blood cells, 4,010,000; white blood cells, 28,900; hemoglobin, 65 per cent; neutrophiles, 81 per cent; lymphocytes, 18 per cent; and monocytes, 1 per cent. During the two months of the child's hospital stay the red blood cell count and hemoglobin values remained essentially unchanged. The white blood cell count dropped gradually to 7,600, and his polynuclear cell count to 20 per cent. The blood Wassermann was negative.

A biopsy examination of a section of deltoid muscle showed arteriolosclerotic changes in the blood vessels. The following report was made by Dr. Arthur D. Waltz, Pathologist to the Children's Hospital:

"The gross specimen, a small piece of tissue 5 mm. in diameter, appears to be normal muscle. Microscopically the muscle fibers do not show any pathological changes. The arterioles show relatively thick walls with a narrowed lumen. Special stains fail to demonstrate any increase of fibrous connective tissue in the wall. The thickening of the wall is apparently caused by an increase in the muscle of the media."

Three weeks after his hospital admission this child slowly developed, over a period of two or three days, a hemiplegia involving the left side of the face and left arm and leg. This was unaccompanied by signs of cerebral shock. Spinal fluid obtained by lumbar puncture revealed a normal, colorless fluid. On the other hand, a subdural puncture at the right angle of the anterior fontanel (right side of the brain) procured a xanthochromic fluid, indicating that a subdural hemorrhage had

occurred. At no time was there any evidence of increased intracranial pressure. There was gradual but incomplete improvement of the hemiplegia over the next few weeks.

One month following the onset of the hemiplegia, an encephalogram was made, which showed an extensive degree of advanced generalized brain atrophy (large areas of subdural air collections and dilatation of the ventricular cavities).

With this marked degree of cortical change it was surprising to have the psychologist find the child of normal mentality for his age. The following is the report of the psychologist, Dr. Phyllis Blanchard of the Philadelphia Child Guidance Clinic:

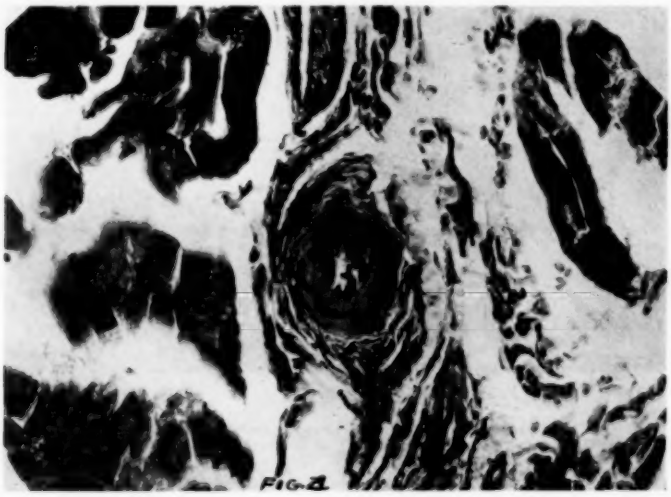

Fig. 4.—Microphotograph of biopsy section of deltoid muscle (C. H.), showing arteriolosclerosis. (×640.)

"I used the Gesell tests of mental development with C. H. In responses to play materials, reactions to people, in the use of his right hand and arm, ability to carry out simple verbal instructions (such as "hand me the cup" or "throw me the ball"), C. H. tests at the twenty-four months' level. His life age is twenty-two months (born 3/25/36). With respect to locomotor development and speech development, however, he tests only at the nine months' level. The lack of locomotor development is of course understandable with the paralysis of the left leg and arm. I would assume that the retarded speech development is the result of his physical condition. There is a real question as to what this will mean for his future development. I would say that at present, he is a normally intelligent child, who is unable to express himself verbally. If he does not develop ability to speak, but remains with a language handicap such as this one, there is a question as to how much this may interfere with his whole mental development, in which language communication plays such an important part as the child grows older. If he can recover from his physical difficulties sufficiently to be able to achieve a fairly normal speech development, the prospect for his mental development is probably better."

Four days after the encephalogram was performed the child developed and recovered from an upper respiratory tract infection.

The patient was removed from the hospital by the parents against our advice. At this time the hemiplegia had cleared somewhat, and his general condition was improved. There was also a small gain in weight, but his blood pressure remained at the same high level. We were told by the family physician that this child died three months later of a questionable pneumonia.

Fig. 5.

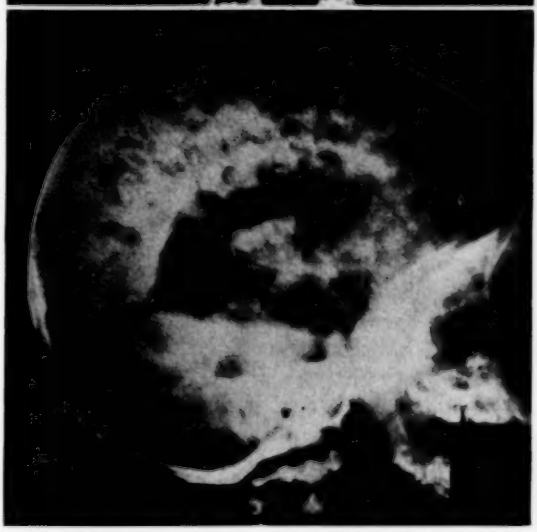

Fig. 6.

Figs. 5 and 6.—Encephalograms taken one month following hemiplegia, showing advanced degree of cortical atrophy.

DISCUSSION

The sequence of events occurring in this patient following the establishment of his hypertension was clear and easily explainable. The

cardiac enlargement was most probably a work hypertrophy, and cerebral hemorrhage is a common sequela of vascular disease with hypertension. While the occurrence of cerebral cortical atrophy as a result of arteriolosclerosis must be infrequent, nevertheless, in the presence of cerebral cortical atrophy, the possible coexistence of arteriolosclerosis should be considered. From the encephalographic studies it is obvious that the patient presented here had a very widespread cerebral atrophy. (Note the roentgenograms showing very wide sulci and dilated ventricles.) This is in accord with the pathologic findings in the brain in malignant hypertension, as noted by Rosenberg [2] in a study of seventeen cases, one a boy of 7 years of age. This author found that multiple diffuse miliary infarcts and hemorrhages were the common cerebral lesions. He further demonstrated the presence of multiple minute cystic formations which could easily be the basis for the cerebral atrophy. It is worth repeating that our child, in the presence of such advanced cortical atrophy, had an estimated normal intelligence.

It is difficult to define clearly the cause and the events leading up to the establishment of this child's hypertension. From the clinical data available, the two most likely etiological possibilities which present themselves as explanations are idiopathic malignant hypertension and primary renal disease with a secondary elevation of the blood pressure. The finding of a hydronephrotic right kidney in the roentgenogram was the only unequivocal evidence to suggest the existence of a kidney disturbance as the basis for the hypertension. Other evidences which suggested that the kidney was involved, but which were by no means conclusive, were the following:

1. The history of an elevated blood urea nitrogen (92 mg. per cent) prior to admission to the hospital.
2. The occurrence of pyuria on four occasions.

There are circumstances, however, which would render these findings questionable as indicators of kidney disease. It is to be remembered that, at the time when the blood urea nitrogen was found to be elevated, the child was said to be extremely dehydrated and to have had an obstruction of the urinary stream because of an ulcerated meatus. It is well known that dehydration in a young child[3] can produce urea retention of a marked degree. Furthermore, the urinary obstruction itself could cause a similar retention of urea. The fairly rapid return of the urea nitrogen to a normal value in seven days is in keeping with what is known to occur after the relief of an acute obstruction to the urine flow, or to hydration of a previously dehydrated infant. This rapid decline in the blood urea nitrogen indicated that the existence of any severe renal disease was unlikely at the time of his hospital admission.

The finding of pyuria could be accounted for by the existing local meatal infection, since the pyuria disappeared and the urine was sterile following the healing of the meatal ulcer.

Nevertheless the hydronephrosis of the right kidney was a distinct abnormality. Cystoscopic examination and catheterization of the ureters failed to show any obstruction, even though the pyelograms showed an apparent constriction at the right ureteropelvic junction. Urine specimens obtained from both ureters showed no abnormalities. In the absence of any concrete evidence, the assignment of a definite cause for the abnormal renal pelvis would be entirely speculative. It is also to be remembered that the renal function, as measured by P.S.P. excretion, was entirely normal. Thus, we are unable to state that there was a definite etiological relationship between the hypertension and the renal abnormality encountered.

The data presented by Weiss and Parker[4] would seem to be a priori evidence that this relationship was lacking, for these authors suggest that generalized arteriolosclerotic changes are not likely to occur in association with the hypertension of pyelonephritis. They state, "The vascular lesions in chronic pyelonephritis are restricted mainly to the kidneys, in contrast to those in 'primary' malignant hypertension, which are generalized."

We believe, however, that this viewpoint of Weiss and Parker is untenable in childhood and that generalized arteriolosclerosis can result from pyelonephritis in children. In support of this, we are presenting the following data:

CASE 2.—V. P., a 6-year-old white boy, was admitted to the Children's Hospital of Philadelphia on the service of Dr. James J. Reilly on April 18, 1933. He was found to have a marked arterial hypertension (blood pressure 260/210) in association with clear-cut evidences of pyelonephritis (pyuria, colon bacillus bacilluria, low renal function, and urea retention). Death resulted from cerebral hemorrhage on Sept. 15, 1933. Autopsy revealed the following: Congenital valve of the posterior urethra; dilatation and hypertrophy of bladder, ureters, and kidney pelvis; chronic cystitis, ureteritis, and pyelonephritis; complete inflammatory destruction of right kidney. The examination of the small blood vessels in sections of deltoid muscle as reported by Dr. Waltz was as follows:

"Microscopically there are changes in both the muscle fibers and arterioles. Some of the muscle fibers are without striations, swollen and of a smooth hyaline appearance. Two types of changes are noted in the arterioles: one a general thickening of the vessel wall apparently involving only the muscle of the media, the other an irregular thickening of the wall encroaching on the lumen from one side, and finally occluding the vessel entirely as shown by sections at different levels. These areas show much connective tissue as well as muscle fibers."

Of the cases of arteriolosclerosis recorded from the pediatric literature by Guild, Kindell, and Gibson,[1] two had active urinary infection associated with arteriolar changes outside of the kidneys, and three others had pyuria with similar arteriolar changes. In one of their own cases there was a diffuse pyelonephritis associated with extra-renal arteriolar changes. In their second case with arteriolosclerosis, pyelonephritis was

not found at autopsy, yet the patient had a distinct pyuria and urinary tract infection during life. Similarly, Butler[5] reported arteriolosclerosis in the one case of pyelonephritis with hypertension in which the small peripheral vessels were examined. The finding of arteriolosclerosis is

Fig. 7.

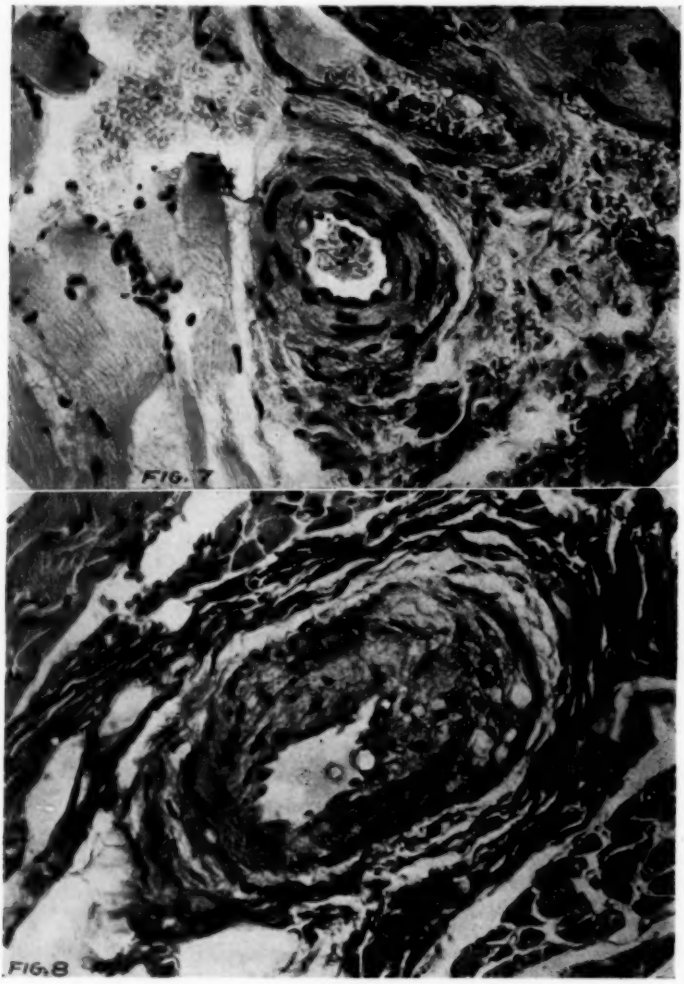

Fig. 8.

Figs. 7 and 8.—Microphotographs of peripheral blood vessels (V. P.), showing arteriolosclerosis. (×640.)

therefore not sufficient evidence to exclude pyelonephritis as the basis for persistent hypertension in childhood. Some analogy may be drawn also from Goldblatt's experiments, for he has demonstrated that, following the prolonged interference with the kidney circulation, generalized arteriolosclerosis did occur.

Weiss and Parker have reported cases of healed pyelonephritis where changes in the renal blood vessels persisted after the disappearance of the active kidney infection. In these patients with "healed pyelonephritis" the hypertension also persisted. The summary data in our 20-month-old patient offer little to demonstrate the existence of an undisputed kidney infection at any time. We are, therefore, left with the alternative possibility that there existed a so-called idiopathic malignant hypertension in this patient.

SUMMARY

The case record of a 20-month-old male infant with arteriolosclerosis is reported.

As a complication of this disease an advanced degree of cerebral cortical atrophy occurred. It is emphasized that in the presence of cerebral cortical atrophy in childhood, arteriolosclerosis should be considered as one of the less common etiological possibilities.

The possible causes of the hypertension and arteriolosclerosis in this child are discussed.

In contrast to the adult, the child with chronic pyelonephritis and hypertension often has diffuse arteriolosclerosis.

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INTRAPERITONEAL HEMORRHAGE CAUSED BY STRANGULATION AND RUPTURE OF A NORMAL OVARY IN AN 8-YEAR-OLD GIRL

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THE immature ovary of a child seems to escape the majority of vicissitudes which may affect the mature organs. When the normal ovary of an 8-year old girl becomes strangulated by torsion of its pedicle, and when it ruptures, producing a severe intra-abdominal hemorrhage, it constitutes such a bizarre emergency that it merits reporting.

M. B., a white girl 8 years of age, was admitted to the hospital because of severe abdominal pains. Forty-eight hours prior to admission, while jumping rope, she was seized with violent abdominal cramps. She described the sensation "as though someone had kicked me in the stomach." The pains were so intense and the abdominal muscles so spastic that she "could hardly breathe." The acute paroxysm lasted for about one hour and suddenly stopped. By the time her physician arrived, all semblance of pain and rigidity had completely disappeared. He advised that she remain in bed, but the youngster felt so well that she was soon playing with the other children.

Thirty-six hours later, while dressing for breakfast, she experienced a second attack. The abdominal cramps were so agonizing that she resented any effort to move her. She experienced a sickening nausea and vomited almost continuously for two hours. The respirations were quick, shallow, and grunting. Any attempt to take a deep inspiration resulted in an annoying discomfort in both supraclavicular spaces. Three hours later the cramplike pains suddenly subsided, leaving only a slight residual soreness in the lower part of the left abdomen.

She did not appear acutely ill on entrance to the hospital. Her temperature was 101.8° F., and the pulse rate was 110. Respirations were definitely embarrassed because of diminution of diaphragmatic excursions, but examination disclosed no evidence of pulmonic infection. The entire abdomen was somewhat tender and the muscles of the left flank were slightly spastic. Peristalsis was very active. On bimanual examination, a tender mass was found to be lying posterior and to the left of the infantile uterus. Proctoscopic studies revealed a decided bulging of the anterior rectal wall as though it were being pushed inward by some extrinsic mass; yet its mucosal lining appeared normal.

The stools and urine were negative for pus and blood. There were 21,000 leucocytes, of which 88 per cent were of the neutrophilic variety. A preoperative diagnosis of a ruptured ovary with intraabdominal bleeding was suggested by Dr. Rasmussen, but we both concluded that the appendix had ruptured, producing a localized peritonitis.

As soon as the abdomen was opened, approximately 100 c.c. of bright red blood escaped. The peritoneum was hyperemic and inflamed. The appendix hung over the brim of the pelvis and appeared normal. The cul-de-sac contained a dark, hemorrhagic mass of tissue consisting of the left tube and ovary which had become strangulated by torsion of their pedicle. These organs were tense, firm, and gan-

From the Surgical and Pediatric Service of Bishop Groves Latter-Day Saints Memorial Hospital.

grenous. Bright red blood was seen escaping into the peritoneal cavity from a rent in the ovarian capsule (Fig. 1).

The actual removal of the strangulated ovary and Fallopian tube was not difficult. A tranfixion ligature was placed around the pedicle, proximal to the point of torsion, before releasing the "twist." This maneuver prevents the emboli and toxic products from entering the systemic circulation. Davidson[1] denounced the folly of disentangling the twisted pedicle before occluding vessels, as he felt that such a practice invited unfavorable embolic reactions. No attempt was made to aspirate the hemorrhagic fluid because the mechanical cleansing of the peritoneum seems to produce more adhesions than does the spontaneous absorption of the extravasated blood. Her convalescence was uneventful, and she returned home on the sixth postoperative day.

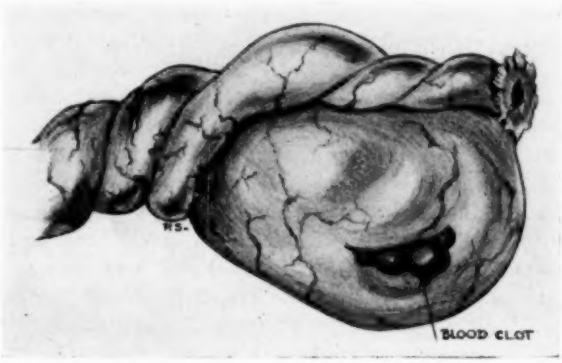

Fig. 1.—Edema, vascular congestion, gangrene, and spontaneous rupture of a normal ovary, resulting from a complete torsion of its pedicle. Observe the blood clot protruding from the lacerated ovarian capsule.

Pathologic Report.—The specimen consisted of a gangrenous ovary and Fallopian tube. The ovary measured 2.5 by 3 cm. The purplish serosal covering presented a serrated laceration measuring 1.5 cm. in length, from which protruded a well-organized blood clot. The Fallopian tube was patent throughout, but its walls were gangrenous and impregnated with extravasated blood.

The cut section of the ovary appeared as a homogeneous blood clot, with none of the normal stromal markings visible. Microscopically, however, the morphologic pattern was perfect. The stroma contained many small primordial follicles, a few of which presented vacuoles resembling minute cysts. There was a diffuse hemorrhagic infiltration of all component tissues. The salpinx presented the picture of venous congestion with early gangrenous degeneration. The spontaneous rupture of the ovary had apparently been produced by the increased intracapsular pressure resulting from the vascular stasis.

DISCUSSION

This case is unique: first, because a normal ovary and salpinx seldom become strangulated; second, because a spontaneous rupture of a normal ovary is rare; and third, because the infantile female organs usually escape such dramatic accidents. Northcutt and Baron[3] describe the case of a 7-year-old girl in whom they found an intraperitoneal hemorrhage caused by the spontaneous rupture of a strangulated ovary.

They cited thirteen instances in which normal ovaries had become strangulated, but in none of them was there an associated hematoperitoneum.

Torsion most frequently affects the adult ovaries, particularly those which have undergone pathologic enlargement. In children, Mayo and Butsch[2] found that strangulation affected only those ovaries which had undergone cystic, teratomatous, sarcomatous, or carcinomatous transformation. The supporting ligaments of the undeveloped juvenile generative organs are so short and wide that the dangers of torsion are reduced to a minimum.

There are no pathognomonic symptoms attending this dramatic crisis. While pain is always present, it is so variable in duration, intensity, and location that it possesses little diagnostic value. The onset may be insidious, with a mild, noisome discomfort centering in the lower abdomen which gradually increases in severity. This usually indicates an incomplete torsion of the pedicle, with a progressive vascular stasis. Sudden, sharp, cramplike pains signify a complete occlusion of the pedicle, with inevitable gangrene of strangulated tissues. Cessation or diminution of the pains may be due to a spontaneous release of the torsion or to a loss of viability of the involved structures. In our case, an interval of thirty-six hours was required for the gangrenous change to take place, during which period the patient was free from pain. The second paroxysm announced the rupture of the ovary, with the resulting hematoperitoneum.

Nausea and vomiting are seldom present, and if encountered, they indicate either a peritonism or a reflex shock from the sudden strangulation of a viscus.

Physical examination may be very informative, or it may give no hint concerning the provocative cause of the "acute abdomen." Pain, tenderness, and muscular rigidity are invariably present, but they possess little diagnostic value. In young children, the pelvic cavity is very shallow, and one can usually make a satisfactory palpation of all the contained viscera by inserting one finger into the rectum and compressing the impinged organs against the other hand which is resting above the pubis (Fig. 2). By this procedure, we found the offending mass occupied the left side of the cul-de-sac and was intimately associated with the uterus. It did not present the "soft and doughy" texture of a hematoma nor did it fluctuate as a pelvic abscess. It is well to remember that a localized cul-de-sac abscess lies behind the uterus and bulges into the lumen of the rectum, producing an inflamed, succulent mucosa. Should an abscess or hematoma be suspected, a colposcopic or proctoscopic aspiration of the fluid usually permits an accurate differentiation.

A correct diagnosis of a strangulated ovary can be made only after eliminating several mimicking diseases. If one suspects an intussusception, a roentgenologic study of the gastrointestinal tract is imperative.

Scout films of the abdomen occasionally reveal the presence of free fluid, dermoid cysts of the ovaries, solid tumors of the generative organs, renal calculi, and intestinal obstruction. Strangulation of the right ovary is invariably mistaken for an appendiceal abscess or a localized peritonitis. One should always be mindful of primary peritonitic infections and of pelvic inflammatory diseases of childhood, for these ailments are not always surgical problems.

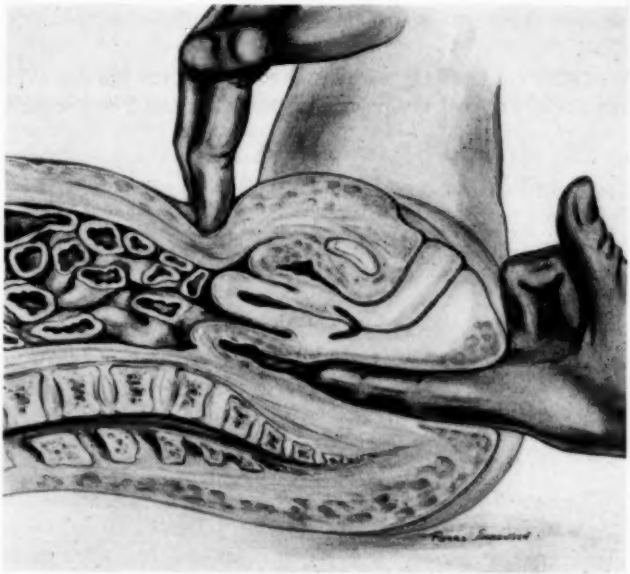

Fig. 2.—Method of palpating the pelvic viscera in a child. The shallow juvenile pelvis favors this procedure.

It is imperative that careful microscopic studies of all excised tissues should be made, for Witzberger and Agerty[4] found that 38 per cent of all ovarian tumors in children were malignant. When one realizes that 98.8 per cent of all torsions and strangulations affect the pathologically enlarged ovary, the wisdom of such caution is apparent.

SUMMARY

Torsion and strangulation of a normal ovary and Fallopian tube, complicated by spontaneous rupture of the ovary and severe intra-abdominal bleeding, which occurred in an 8-year-old child, is reported. Only one other similar case has been described in the literature.

Pain is the most constant symptom, but it is so variable in location, intensity, and duration that it possesses little diagnostic significance.

Bimanual rectal and abdominal palpation frequently locates the offending organ and establishes its relationship to the uterus. Neoplastic enlargements of the ovaries can be determined by this maneuver.

Torsion and strangulation of the ovary must be differentiated from pelvic peritonitis, acute salpingitis, inflammatory, cystic or neoplastic enlargement of the ovary, intussusception of the bowel, acute appendicitis, and appendiceal abscesses.

Crushing clamps or transfixion ligatures should be placed on the gangrenous pedicle proximal to the point of torsion before any attempt is made to release the strangulation or to remove the ovary. This minimizes septic and embolic reactions which may be produced if the material from the degenerating organs be given free access to the systemic circulation.

It is imperative that the strangulated structures be studied microscopically, as 38 per cent of all ovarian tumors in children are malignant.

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WOUND DIPHTHERIA IN THE NEWBORN INFANT FOLLOWING CIRCUMCISION

Report of a Case

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WOUND diphtheria is not an uncommon postoperative complication. Grossman and Radice,[5] taking 700 smears from 400 wounds, found the diphtheria bacillus twenty times. It was most common in wounds with a tendency to poor healing. In fact, the diphtheria bacillus was found when it was least expected. Fresh wounds apparently favor the growth of diphtheria bacilli.

Frankenthal[4] states that, in the investigations of 186 nonsuspicious wounds, diphtheria bacilli were found in twenty cases (10.7 per cent). These were, however, secondarily infected operative wounds. These cases had gray-yellow exudates with very poor tendency to healing. In some cases erysipelas played an exceedingly important role, since it preceded the bacillus infection. Other bacteria, such as streptococci, staphylococci, and pyocyaneus, have been found as mixed infections.

The case of a child, 21 months of age, who, after having been vaccinated against smallpox, developed wound diphtheria in the thigh, is reported by De Haas and Wolff.[3] The diagnosis was confirmed both bacteriologically and by animal experiment. Recovery followed the use of antitoxin.

Linde[7] in 1934 reported a case of a 74-year-old woman who had diphtheritic or diphtheroid infection of the wound following appendectomy with fatal termination.

In 1932 Nigam,[8] subsequent to the removal of a rib for tubercuious caries, found the diphtheria bacillus in the exudate around the sinus. The glands in the axilla and groin were enlarged and painful. Prompt treatment with antitoxin and antiseptic dressings locally brought rapid relief.

Wound diphtheria following circumcision is reported by Hasbrouck[6] in a 3-year-old child. The indication for circumcision was a tight prepuce with very little opening. Following the circumcision, 2 per cent carbolized oil was applied. About forty hours later an exudate was observed covering the wound area, and erysipelas was spreading rapidly to the abdominal wall. Cultures from the throat and wound proved to be diphtheria. The patient died on the eighth day.

Another case of diphtheria of the penis is reported by Bailey.[1] In this instance, the patient, a barber, aged 26 years, consulted the physician for the complaint of swollen penis. A foul-smelling exudate was noted within the sulcus. The culture proved positive for Klebs-Löffler bacillus. Antitoxin was administered, and the patient made an uneventful recovery.

REPORT OF CASE

E. P. was born on June 11, 1940. He was a first child, and delivery was normal. His weight was 3,430 Gm. His general condition was good. The genitals were normal, and the skin was clean.

The parents requested circumcision, and this was performed on June 19 by the family physician who delivered the infant.

The following day, June 20, 1940, the infant was sent home with the notation on the chart that the circumcision was healing and that the baby was in good condition.

On July 30 the infant was brought to my office because there was tendency to poor healing of the circumcised area. Examination was negative except for related findings.

To the right of the umbilicus, about 1 cm. away, a small area of denuded skin with an exudate was noted. At the frenal area of the penis was an exudate about 1 cm. in diameter and very adherent. It was impossible to remove this exudate entirely. The skin surrounding the corona and shaft was edematous, swollen, and painful. The inguinal glands were somewhat enlarged.

A small amount of the removed exudate was sent to the laboratory for culture. The following day the report came back as positive for Klebs-Löffler bacillus.

Treatment.—Ten thousand units of diphtheria antitoxin were injected into the right gluteal region, and local wet antiseptic dressing was applied. On August 3 definite separation of the exudate around the edges of the wound was noted. The exudate to the right of the umbilicus also was separating. By August 8 the wounds were clean and practically healed. Recovery was complete.

COMMENT

The source of this Klebs-Löffler infection could not be traced. Examinations of parents and aunt of this newborn infant were found to be negative. At the hospital, all the nurses have periodic throat cultures taken, and any nurse who complains of any soreness of the pharynx is immediately removed from the nursery. The setup for circumcision is ideal, since all dressings, instruments, and sutures are sterilized in a container and kept sterile. The physician who performs the circumcision is required to prepare as if for a major operation. The belief is that the wound became infected at home, perhaps from clothes, dressings, or the hands of persons who changed the daily dressings.

SUMMARY

A case of wound diphtheria following circumcision is reported.

The infection occurred in a breast-fed baby in the newborn period of life, an unusual time. After six weeks of nonhealing, complete cure was effected by the administration of diphtheria antitoxin.

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THE PERIOD OF RESISTANCE IN EARLY CHILDHOOD

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THERE are two periods of childhood during which a child's education becomes something of a problem. One of these is adolescence which begins at different ages depending upon race and living standards. In the white race and with our own climatic conditions, it starts between 13 and 14 years of age. Within this time many children are difficult to handle; they have a strong will of their own and are no longer inclined to follow the orders of their parents. Other children have difficulty in maintaining contact with their environment. They seek solitude, write poetry or stage plays, and sometimes construct peculiar philosophic systems.

Adolescence is a normal period of the child's life which lasts a relatively short time. Often, however, there are pathologic reactions which make the study of adolescence most important for the pediatrician and the child psychiatrist. After adolescence, the interrupted equilibrium of personality is re-established, but the background of personality has changed in many respects.

Most people are informed about adolescence, but only a few know that there is also in early childhood another period during which many children are difficult to handle. If we talk with mothers about the development of their children, many of them will tell us that in the second or third year of the child's life there is a period during which the child is inclined to say "no" to everything and shows a tendency to refuse all commands of the adults. If the mother wants to take a walk with the child, he insists on staying at home. If relatives come around, he will not greet them. If he is to take his milk, he wants cocoa. In brief, the child is in a contrary state of mind which manifests itself sometimes drastically by stormy scenes of resistance. This period of life lasts under ordinary circumstances only a few months, and afterward the child is no longer an educational problem.

There are children, however, who have serious difficulties during this period of their life and who are in danger of becoming abnormally disturbed in their development. Because of the general lack of knowledge about problem children during early childhood, I have made my own study of the matter since 1930. It was my hope that such research might not only clear up the problem of the psychopathology of early childhood but also lead to a better understanding of some reactions of older children. In early childhood many reactions of the child are very easy to understand because at this stage of life he is not able to conceal his intentions. We can see through his reactions and study

them with greater accuracy than in later life. Here we have a simplified model of most of the reactions we meet in the large field of child psychiatry.

But if we wish to study this problem, we must examine the small children not only in the consultation room. It is necessary also to live with the little patients day and night. We must know many things which cannot be told by the mother. The method which I find advisable is a very inconvenient one, but other more convenient methods lead only to misunderstandings. We must study personally and not merely by description the behavior of such children in a group or when left alone. We must study their play activities, their dependence or independence, their methods of feeding, modes of dressing and undressing, habits of sleep, and so forth. He who would avoid these inconveniences had better work in another field of medicine. It is no disgrace at all for a physician to work for a time as an educator or even a nurse.

The first patient whom I would describe is a girl 2 years and 6 months old. She has a sister who is 13 months old. During the first year of the child's life there were many difficulties concerning her bringing-up. She was troubled with loose bowels and she did not like to take the bottle, which she rejected for weeks. Therefore, excellently trained nurses were engaged for her. Nevertheless she lost her appetite. Her feeding was a trial for all concerned because the child continually fussed and cried. Ultimately the scenes were accompanied by vomiting spells, through which she apparently sought to domineer those present by arousing their sympathy and concern.

Other facts will aid us in our study of the case. Since infancy the child had been restless. Later on she became resistant to an extreme degree. Taking a walk with her nurse, she ran away and threw herself on the streetcar tracks, compelling the streetcars to stop. She broke her sister's nursing bottles and poured the contents into the garbage can, saying that her sister should also starve if she herself refused her meals. But secretly she went to the kitchen and ate from the garbage.

The family took this child from her homeland, Czechoslovakia, to three or four of the most outstanding pediatricians living in Germany; but these consultations came to an unhappy end because the child could not be examined and instead destroyed in her rage some valuable instruments of the respective physicians. Finally she arrived at my own clinic. The mother brought her but had to leave very soon because there occurred one temper tantrum after another. During the first meal spinach was served, which unfortunately the child did not like. She looked suspiciously at the dish and shook her head. For supper the other children received cocoa. When our patient began to drink out of her cup, she observed that in it was the cold spinach from lunch. She looked around very much astonished, but did not cry. She put the cup on the table and observed the other children, who drank the cocoa with excellent appetite. Next morning breakfast went along in the same

way; but when the spinach came on the table for the fourth time for lunch, the child was willing to eat it. Later on there were no more difficulties with feeding. Instead the child began soiling her clothes, perhaps as a drastic demonstration against our rather cruel educational methods. The spiteful rebellion lasted nearly three months; then it disappeared. The little girl played well with other children and was no longer difficult to manage. But she was always a little fearful, did not like to be alone, clung to the adults, and wished always to be the center of attention. After the patient was discharged, her progress continued. The parents, however, took home with them one of our nurses, who was able to get along with the child. But naturally the disposition for that sort of spite reaction was there, and we heard that it was still present when the child was 14 years old, although she was in other respects a nice and well-trained girl.

I got the impression that the various nurses who were with this child during the first year of her life were in the main responsible for the terrible situation. Such trained nurses are sometimes a serious impediment to a child's development. Many nurses have not at all the right understanding for the psychical needs of a child. They think that they are doing enough if they take care of his physical health.

I personally think this case presents a lot of problems. How can a small child develop such terrible obstinacy that streetcars must stop and that dignified and famous doctors must tremble in behalf of their equipment? How can we understand the maliciousness of the child against her small sister? Could there perhaps be some connection between the feeding difficulties and the resistance?

We meet these and many similar questions in nearly all cases with such children, and we must answer that the psychology of small children has quite a different aspect from the psychology of older children or adults. The child, during the first two or three years of his life, is not a very rational human being, but is ruled by emotional reactions and instincts. Thus, the behavior of such small children reminds us very much of some primitive reactions; for example, the storm of movements observed with infusorias or the fluttering of a frightened little bird which has caught itself in a room and flutters against the walls and windows in a state of extreme and senseless anxiety. There is no thought in this child about his reactions; all is instinctive, emotional, and very primitive.

It would be worth while to analyze the spite reactions of such children because spite obviously occupies the very center of the whole picture. We have seen it in the previous case, and, furthermore, we know that this period of life has been called the "spite period," "period of remonstrance," or "Trotzperiode des Kindesalters."

If we do so, we will discover that the most impressive reactions of resistance are nothing more than a screen behind which something else

is lying. I can imagine two men in a discussion in which they become somewhat excited. Suddenly one of the men loses his composure, bangs his fists on the table, and shouts, falling into a real temper tantrum. In such a situation one can predict with great accuracy that the latter does not have the best arguments and that his behavior is caused by his inner insecurity. Nobody falls into a temper tantrum who can defend his case with good arguments.

This is an example taken from the psychology of adults. But during childhood there are similar conditions. Behind the screen of spite reactions, such as temper tantrums, there is always anxiety or inner insecurity. Whoever has the chance to observe children from early morning until night will soon recognize the importance of these phenomena. In the case of one child, the mere thought of Santa Claus causes boundless eagerness to arise. In the case of another, the swallows flying through the house become a source of fear. A third trembles while walking to the gymnasium, clinging to the adults and crying if he is ordered to perform a harmless exercise. One could also tell of how suspiciously and anxiously the child meets his playmates, how darkness, uncanny noises, dogs, or other harmless animals arouse his anxiety, and how this trait manifests itself during sleep and in dreams.

Such anxiety may not always be evident, but it is always present. Two- and three-year-olds of this disposition are often in a terrible state. Anxiety governs their whole life. Both day and night this anxiety is present, and sometimes the unhappiness of the child expresses itself very clearly in sad and even tormented features.

On the background of anxiety or inner insecurity arise the famous spite reactions and the temper tantrums. One child gets mad every time he is crossed. Another screams and yells at the slightest provocation. And in many cases there is a real storm of excitement into which he is drawn, leading to even more violent and explosive reactions. Many children throw themselves on the floor, bang their heads against it or against their mattress, slam doors, stamp their feet, throw things at people, direct their rage against themselves by striking themselves, knock their heads against the wall or the table, hurting themselves badly, attack adults, or hit their mothers. Such severe temper tantrums may be climaxed by real convulsions.

One must agree that the temper tantrums which I have described just now are most impressive phenomena, but nevertheless we must study them in their proper perspective. The temper tantrums are really only a show! The child is playing the part of a wild man and most adults will be deceived by his attitude.

The normal way which the child has to follow during the first years of his life is the way of the community. Even the infant has a few social tendencies. For example, he cries if another child is crying, and he seeks contact with his mother. But these relations enlarge themselves

during the second or third year of the child's life. He begins to play with one or more children. Later on he mingles with a larger group. The play must then have some rules, which are to be followed by every child.

Unfortunately, with our group of problem children there is another way. These children are not able to adjust themselves to other children. They have instead the tendency to fight with their playmates and to hit them. Some children delight in teasing or tormenting their comrades by throwing things at them, or are even inclined to bite. It is understandable that the other children won't play with these unruly youngsters and that they are afraid of them. Many of the children are not interested in group activities. They do not like a group, prefer to play alone and stand around in the nursery school. Then there is often the child who is derided by his playmates because they have the feeling that he is too anxious and bashful. They abuse and tantalize him, making quiet and peaceful play impossible. Some children play well if they can be ringleaders; otherwise there is a fight. Others like to play only with younger or older ones because they can command the first group or put themselves under the protection of the second. In connection with social behavior we should also mention the important problem of jealousy between siblings. I have come to the conclusion that this point cannot be overestimated. In many cases it is the key to the picture.

The inability of such children to adapt themselves to the life of the community is one of their most important features, especially from the practical point of view. In all cases disturbances like the above are present. We are forced to question seriously the possibility of adaptation to the life of the community if the child has failed to adapt himself during the first years of his life.

Only a few physicians will tell us something about the anxiety of such children or about the difficulties arising through their inability to adapt themselves to the life of the community. But nearly all physicians know something about the so-called symptoms, which seem to be much more important than anxiety or other similar reactions. These symptoms attract medical attention easily; but they are really only outward manifestations of the child's psychical situation. Here we meet the well-known and very disturbing difficulties of feeding and forms of vomiting which seem to be rather arbitrary. We notice also the frequency of different forms of disturbances of speech, among which the more or less delayed development of speech, stammering, and disturbances in building up sentences play a prominent part. Stuttering also plays its role. Delayed habits of cleanliness and enuresis and encopresis belong not infrequently to the picture of the pathologic type of the spite period, as well as disturbances of sleep, which are also common, manifesting themselves as nightmares, insomnia, anxiety dreams, or otherwise. There is, moreover, the tendency to many habit formations and stereotypical reactions, especially thumbsucking, pulling and sucking

on the bed linen or the lips, licking the body, scratching the skin, and rocking the head during the night. Here we meet also masturbation, which may be more frequent than our records let us suppose. Motor inhibitions of different kinds are frequently present. There are also breathholding spells whose psychologic connection with spite reactions seems to be evident.

These symptoms are of great importance to the whole picture because they demonstrate clearly that something is wrong with the child. We are interested in the symptoms not because of the medical problems such as feeding difficulties or disturbances of sleep; rather we are interested in the symptoms because they prove that the patient is not on the right road to adapting himself to the life of the community and because we are afraid that his psychical development is in danger. Our goal is to understand these manifestations which have been called with good reasons a form of "speech of the organs." An analysis of the symptoms is nothing but a partial analysis of the whole personality. The explanation for it lies in the following facts. Every psychical emotion has an influence on the body. As we know, the small child jumps around and sings with great pleasure if he is happy. Contrariwise, he screams and cries or perhaps hangs his head if he is sad or discouraged. The child is unable to hide his feelings. Body and soul in the first years of the child's life are in closer unity than later on and therefore every psychical emotion reacts openly on the body. Here there is an understandable explanation for the origin of the symptoms during early childhood and perhaps also during the later life of the child.

We have mentioned the most important features of such children and we have now to ask the reason for anxiety. If we gain a right understanding of anxiety, we shall also know why it might be difficult for such children to adapt themselves to the life of the community.

If a person comes into a strange environment where nobody is friendly to him, but instead, haughty and icily polite, he will lose his inner security and courage, will perhaps become homesick, and will no longer be able to go ahead with his work.

I suppose that something like this happens with our group of children. Usually we have to deal with children who have no brothers or sisters or only one brother or sister. For such youngsters it is more difficult to adapt themselves to the life of the community than for those who grow up within a large family. Furthermore, we have to deal very often with parents whose marital life is not happy. A child growing up in such a tense atmosphere cannot develop well. Finally, the mothers of such children are often not able to give the unselfish mother's love which is essential to the development of a child. Many of these mothers are naturally selfish, much occupied with themselves, and without warm feeling toward their child. Often before marriage they were employed perhaps as secretary, stenographer, saleswoman, nurse, or

teacher, or perhaps they attended college or a university. After marriage and after the birth of a child, they love their former occupation more than the child, who is often really a hindrance to the mother.

I think we can understand quite well the anxiety of such children and why they are not able to adapt themselves to the life of the community. But there are also other impediments. In our previous case the disturbances began with feeding difficulties even during the first year of the child's life. The same happens in many other cases, and we are compelled to ask very seriously if it might be possible that such disturbances, beginning perhaps during the first weeks of the child's life, can be produced by environmental influences or if our observation indicates that hereditary conditions also retard development. Perhaps we are occupied here with a theoretical question, but in studying a disease I will not limit myself only to the points which are of practical importance.

If anxiety or inner insecurity prevents the child from becoming a part of the community, he has three possibilities for dealing with the situation. As we have seen before, he might react by rebelling against his environment. But he has also other possibilities. One of them is given in the following case.

Herman is a boy 3 years and 9 months old. He has one sister 6 years old. Up to a certain point his somatic development went well, but Herman became in the course of time a little too stout and clumsy. His mother began to care for him like a little baby. The boy, nearly 4 years old now, is not able to form sentences and he speaks a sort of baby talk. Off and on he wets and soils his clothes. His habits of playing are monotonous and his movements remind one of the abrupt movements of an infant, as do his frequent crying and whining. There is no modulation of voice, and to hear his crying would make one think that a little baby was in the next room. He is naturally very fearful and will not join in children's play, and the light must be kept burning whenever he goes to sleep.

I think we can be sure what such behavior means. This child does not react with temper tantrums; nor does he show other reactions of remonstrance; rather he refuses to develop. He seems to be going backward instead of forward, seems to be clinging to early infancy and seems to want to continue his baby life. One could call this kind of reaction either regression or standstill at an early point.

The third possibility for the child's dealing with his difficulties is the reaction of withdrawing into himself or turning away from the unpleasant experiences of his life.

The 4½-year-old boy of whom I will tell has one sister, 6 years old. This boy is easy to educate, but is too delicate and sensitive. He is really always living in a state of anxiety which is not covered by any other form of reaction. Witnessing a harmless theater play, he becomes most

excited when the devil or witch appears. Usually he does not participate in the play with other children, but stands around and is not willing to join them. He is easily hurt, cries on all occasions, and has a tendency to subordinate himself to other children. He is very close to his mother, is jealous if she kisses her husband, and even wants to sleep in the same bed with her. His sleep is restless and disturbed by nightmares. He seems to be living in a fantastic world of his own; he daydreams, is extremely slow, and needs, for meals and other activities, twice as much time as other children need.

These three reactions, *resistance, withdrawing into oneself,* and *regression,* are of great importance for the understanding of such children. There is some schematism in this classification. Usually there is not one single reaction present but a mixture of two or even three. I do not believe that these reactions are pathologic ones, but rather that we have to deal here with normal reactions which take place with any normal child. But there seems to be a big difference between a child who reacts with one temper tantrum after another and one who uses his energy for adapting himself to the community, between a child who becomes a queer and isolated personality and one who withdraws himself only sometimes to his phantasies, or between a child who soils or wets himself like a baby and one who is sometimes childish and inclined to be petted by its mother.

As pediatricians or psychiatrists, we have the task of helping these children and their mothers. The situation seems to be not always so simple, for we know very well that the development of such children is in danger. According to my own experiences, the remnants of the so-called spiteful period last many years. Later on in school, especially, difficulties must be expected which are not very pleasant for the family.

There are some therapeutical possibilities which we should mention. We have shown that the reactions of the child are influenced, in the first place, by environment, and our therapeutical methods are designed to improve the situation of the child. We know that he has difficulties in adapting himself to the life of the community. Therefore, we must try to accustom him to life with other children and adults.

In the first place, we have to teach the mother how to handle her child. In some cases there is an exaggerated spoiling of the child. Under these conditions we will tell the mother that even a child of 2 or 3 years must have some responsibilities and that it is noxious for him to be treated as an infant. He needs a certain degree of independence and must be trained to dress and undress and to feed himself. The mother must learn that the child himself will find the right way if he is allowed to act according to his given possibilities. In many cases he really wants to be independent but is not allowed to be so.

Under other circumstances, the parents think that the will of the spiteful child must be broken. The best method for this purpose seems

to be that of whipping. Therefore, the parents erect a kind of dictatorship, with punishment of different kinds. It seems clear that this is not the right way to lead the child to the community. On the contrary, he reacts against this kind of proceeding sometimes with resistance, sometimes by withdrawing into himself, and sometimes with regression.

Often the child is neglected. The parents have other more important interests. They have to go to social meetings or to card parties and the poor child is a hindrance to their life. If he grows up in a rich environment, a nurse or a colored girl is engaged who takes care of him as a more or less disagreeable duty. If he is living under poor conditions, nobody is there to care for him and he gets the feeling that he is quite alone in this world.

We have to deal sometimes with terrible situations, and it is not easy for us to teach the mother that the way she is doing is wrong. The above-mentioned and other mistakes of education are founded on the personalities of the parents, and, therefore, ideally it should be our task to change the personality of the father or the mother or even both. I personally do not believe that we are able to do so.

Naturally we are able to change some attitudes of the parents toward the child. Often a mother desires to be always with her child, even during the night. Therefore he sleeps in the same bed with her. We will not discuss the reason for it, but we must teach the mother that it is not good for her child to sleep with her, especially if there is room enough for the child elsewhere.

Many times the feeding of the child is a matter of concern. He will not eat and then there ensues a battle between child and parents, accompanied by endless discussions, threats, and punishments. We must remember our own experiences which show that meals should be a pleasure and not a torture. Lack of appetite will never be banished if parents continue their faulty proceedings. But if parents follow our advice and stop the coaxing, we can predict that the feeding difficulties will disappear in a short time, although naturally, many of these children will never become heavy eaters. For us pediatricians this matter is not so important because we do not like stout children very much. A slender child with trained muscles is more welcome.

It may be that somebody will ask, "What shall I do if the child gets a temper tantrum?" This question we can answer with great accuracy. We do nothing. We ignore it. The temper tantrum will pass over sooner or later. The main thing is to avoid temper tantrums by an education which gives the child some responsibility, liberty, and freedom, but at the same time, a great deal of discipline.

We have discussed just now our treatment of some disturbances which are important for the practitioner. But generally the practitioner is pessimistic in dealing with similar questions, and he is sometimes unwilling to occupy himself with the quarrels of parents of problem children. In a rather short time pediatricians have been able to abolish

many deep-rooted mistakes connected with the physical care of the child. Why should we not be able to change some attitudes of parents concerning education? This is a matter of prophylaxis and perhaps schools for mothers would be useful for this important task.

In many cases we recommend the nursery school or the kindergarten. Here the child is for a part of the day out of his own home and learns cooperation with other children. He will be more independent than at home and perhaps more cheerful. It may be an important question whether obligatory attendance at kindergarten would not be useful for all children. For our group of children the kindergarten and the nursery school have sometimes the drawback that the child is there only for a few hours of the day and must return afterward to his home and family. Therefore, in many cases, we must consider a complete change of environment, that is, a children's home. This kind of proceeding is very serious. It is a strong encroachment upon the child's life. He feels deserted during the first part of his stay and gets into a state of disorientation. I myself have had many experiences along this line. Some children who have had clean habits begin during the first part of their stay in the children's home to soil and wet their clothes. They protest in this primitive way against admission into the home. It depends only on the management of the respective children's homes if our measure will be beneficial to the child or not. If we have to deal with a home which is directed in a good and reasonable manner, the difficulties of the child can be overcome, and I state that his admission there sometimes means his salvation. In three or four months he has changed his attitude completely, and if meanwhile the parents have learned something about his training, we have achieved wonderful success.

While speaking on the theme of treatment of such children during the period of remonstrance, I would feel that I was avoiding the main issue if I were to close our discussion here.

What is this main issue? I think that anyone can sense what I am to say. All these children are suffering from the lack of a mother's love, which is the foundation of a child's undisturbed and harmonious development. A mother's love cannot be tested by scientific methods such as the famous intelligence tests; nevertheless, it is there and represents the mysterious background for the child's development. One is entitled to ask if this knowledge is useful for the child and if one can help him by knowing something about the importance of mother-love. And I answer that the pediatrician must teach the mother day by day that it is not the care of the body which is the main thing for the small child but rather the unselfish love and protection of his mother. The whole picture of the psychopathology of childhood and especially the psychopathology of early childhood should have one big headline stating that the child who misses mother-love is in danger.

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Round Table Discussion on Vitamins From the Standpoint of the Practicing Pediatrician

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CHAIRMAN TISDALL.—The program this morning will be divided into four parts. Dr. Bessey will discuss vitamin C; Dr. McCune, vitamin D, Dr. Drake, vitamin K; and Dr. Sebrell will take the whole group of B vitamins.

DR. BESSEY.—Vitamin C or ascorbic acid (the latter name is now preferred) occurs naturally in fresh fruit and vegetables, but also is available and has found wide use as a pure substance. The absence of this vitamin from the diet will lead to the development of scurvy. Well-developed scurvy probably occurs infrequently in this country. However, milder degrees of the deficiency are probably more prevalent than has been realized generally in the past. This, and the fact that recent developments in nutrition emphasize the wisdom of feeding at levels distinctly above those required to prevent deficiency diseases in order to be assured of optimum nutrition, has increased the interest of the pediatrician in the vitamin. Fortunately, the development of more practical and accurate methods of analysis has increased enormously our knowledge of the requirements and distribution of ascorbic acid in the last few years.

There are three points relative to ascorbic acid that might be of particular interest and value to this group. One is the matter of interpretation of blood ascorbic acid values. The other points are the requirements for this substance in children, and the best and most practical method of meeting these requirements.

There are two methods of measuring ascorbic acid in the blood plasma. It can be titrated, or it can be measured by a more objective photoelectric method. It is beside the point to go into the details of these methods this morning. It is the

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interpretation which is most important to this group. It is generally, although not invariably, true that in well subjects the fasting blood plasma levels of ascorbic acid reflect the level of intake of this dietary essential. If the dietary intake is very low, there will be little, if any, ascorbic acid in the plasma. As the intake increases, the plasma value will increase from 0 to about 1.4 mg. per cent, at which point a kidney threshold limits the maximum fasting level by excreting any excess.

There are two levels of ascorbic acid intake which are of special importance: the minimum requirements, that level below which scurvy would appear, and the optimum requirements, that amount above which an increased intake would give no further benefits. What can one learn from blood plasma ascorbic acid analysis concerning these two points? A fasting blood value of 1.0 to 1.4 mg. per cent indicates that the subject is receiving an amount above which any additional would be excreted and therefore is receiving a physiologic maximum. Values between 1.0 and 0.0 mg. per cent indicate a proportionately lower intake. Just what blood level in this range represents a physiologic optimum is difficult to determine and has not been established. Since we lack information regarding this point, it has been the policy of many to recommend an intake which maintains the fasting blood value near its maximum. Although this is probably a higher level than the physiologic optimum, it seems a wise procedure to follow at this stage of our knowledge.

Recent observations on both man and experimental animals indicate that ascorbic acid intakes can be such that no demonstrable amount appears in the blood plasma and yet scurvy does not develop. This means that the minimum requirement (amount just sufficient to prevent scurvy) lies somewhere below that intake necessary to give a blood value. A zero blood plasma analysis means that the ascorbic acid intake is low and therefore should be increased, and that scurvy is a possibility, but not necessarily present. Significant amounts of plasma ascorbic acid eliminate the possibilities of scurvy* and values near the maximum assure optimum nutrition in this respect.

All of the above needs are to be qualified by reminding you that some acute infections lower the blood plasma values even when the intake is at a level usually considered sufficient. This has been interpreted by many as evidence for increased ascorbic acid requirements under these conditions. There are also a few individuals who, although apparently well, give low blood values which fail to rise even when enormous amounts of ascorbic acid are fed. Perhaps it should also be stressed that reliable information and interpretation depend on the accuracy of the analytical method. One could cite many examples of false conclusion based on unreliable analysis.

Although blood ascorbic acid analyses, as you can see, have been of limited help in the solution of the problems of minimum and optimum requirements, they have helped to define a point beyond which additional intakes are wasteful (physiologic maximum). Since an intake of this order is not impractical to reach and it assures a margin of safety, this standard has been widely accepted in place of the unknown physiologic optimum.

A number of carefully controlled laboratory studies on adults in which blood and/or urine analyses were used to establish the physiologic maximum have been reported in the literature. These reports agree well but were done on a limited number of subjects, and only a few children were represented. We have recently studied about one hundred well children (4 to 12 years of age) in this respect. The ascorbic acid intake was established by repeated dietary histories over a period

* It has been reported that scurvy may develop even when the blood plasma level is as high as 0.5 mg. per cent. However, much doubt is cast on these claims by recent, more thorough studies on both man and experimental animals.

of many months. Most of the children had been under the regular care of the nutritional clinic for several years, so their dietary habits, etc., were well known. Blood plasma analyses were done by the photoelectric method. This study showed that those receiving 3 oz. of citrus fruit juices daily, or the equivalent in tomatoes or other potent food sources of ascorbic acid, maintained their blood values near the maximum almost without exception. This means that well children, 4 to 12 years of age, receiving 3 oz. of citrus fruit juices or the equivalent daily, have their ascorbic acid requirements covered with a margin of safety. This represents 40 to 50 mg. daily in terms of ascorbic acid.

I want to re-emphasize the fact that I am talking about the maximum possible requirements. The question always arises as to how much benefit is derived from an intake of ascorbic acid or the other vitamins above the minimum requirement. The answer, from animal experiments, is clear on this point. Up to five times the amount of ascorbic acid which will prevent scurvy in a guinea pig will produce benefits as shown by growth and general health records. Evidence from animal experiments involving the other vitamins also indicates a considerable margin between these two points. Such observations on human beings are not easy to obtain, but they seem to show, as would be expected, about the same results.

What is the best and most practical way of meeting the ascorbic acid requirements? Proper feeding is the answer, because it is not only the most economical procedure, but because foods which contain ascorbic acid also contain many other nutritious materials. Since ascorbic acid is the least stable of the vitamins to ordinary procedures in processing and cooking, it is best to depend upon the most stable and most potent sources, namely, citrus fruits, tomatoes, tomato juice, etc.

The use of pure ascorbic acid, it seems to me, should be confined to conditions in which it is impractical or impossible to give the above foods. Examples would be the case of the very young infant, intolerance to foods, need of parenteral treatment, etc.

Since cooking leads to considerable and uncertain losses, we have come to depend upon the more stable and certain sources to meet optimum requirements, such as citrus fruits and tomatoes. It should not be forgotten, however, that such products as the potato are responsible for preventing many cases of scurvy. Although it is not such a potent source as citrus fruits, it is consumed in large quantities, especially among low income groups, and can easily cover the minimum requirements. At certain times of the year, berries, raw fruits, vegetables, and salads may be taken in sufficient amounts to meet the maximum requirements, but as a general rule, children do not regularly consume enough of these products to reach the maximum level.

I might add that tomatoes are about one-half to one-third as potent as citrus fruits. Dr. Drake tells me that, based on their analysis in Canada, they prefer the one-third figure. There is not a great difference between orange juice and grapefruit juice, although, in general, the latter is usually slightly less potent.

DR. DRAKE.—Would you mind telling us something about loss of vitamin C in storing and cooking of fruits and vegetables?

DR. BESSEY.—Since vitamin C is the least stable of the vitamins, its deterioration in the storage, processing, and cooking of foods is greater than for the other vitamins.

It is difficult to make general statements concerning the stability of ascorbic acid in foods because so many factors are involved. In some products, under ordinary conditions of storage and preparation, it is quite stable, while with other materials, great losses may be involved even when the utmost care is taken. Let me give examples.

Citrus fruits and tomatoes represent two of the most stable as well as most potent sources of ascorbic acid. The losses in storage, as long as the fruit remains in good condition, are relatively small. Oranges retain 70 to 80 per cent of the ascorbic acid over the maximum storage period. Tomatoes may be cooked with but small loss, while fresh citrus fruit juices may sit for several hours without appreciable losses. Both types of products may be canned with small loss and remain stable until the can is opened.

Although fresh, green, leafy vegetables are potent sources of ascorbic acid, considerable losses are usually involved before they reach the table. As much as 25 to 50 per cent may be oxidized during cooking. Large additional losses may also occur due to solution of the vitamin in the cooking water, unless this water is used. The ascorbic acid value may become low in this type of product, even before cooking, by wilting, which causes great losses. In general, the degree of crispness is a rough measure of the ascorbic acid content of leafy vegetables such as spinach, broccoli, kale, etc. This also applies to the salad greens, but of course losses from cooking are usually not involved in these products.

Those products which keep well in storage—potatoes, carrots, turnips, cabbage, etc.—lose their ascorbic acid very slowly. Potatoes retain about one-half the original amount after the maximum time of storage. Although the losses in cooking cabbage are great, potatoes and carrots, if not cooked too long, seem to retain most of the vitamin C.

Freshly grated vegetables show a rapid loss due to oxidative enzymes liberated by breaking of the cells, and they should be used without too much delay.

In general, acidity (citrus fruits, tomatoes), absence of air, and low temperature are favorable to preservation, while overcooking and oxidative enzymes cause rapid destruction.

It is interesting to note that the ascorbic acid content of fruits and vegetables may vary a great deal also, depending upon variety, soil, climate, light, rootstock, etc. As much as 100 per cent variation may occur due to any one of these factors.

MEMBER.—What about pineapple juice?

DR. BESSEY.—Yesterday I gave the rough figure of about one-fifth as potent as the average orange juice in regard to ascorbic acid, and someone corrected me later and said that I had given too high a figure. I would say about one-fifth is a fair figure. You can't depend on it as an important source of ascorbic acid; it can hardly be considered with the citrus fruits or tomatoes.

DR. DRAKE.—Will you tell us about the vitamin C content of other fruits?

DR. BESSEY.—In general, the content of other fruits is considerably lower. For example, the grape has practically no vitamin C in it, so grapejuice is unimportant in this respect. We have already spoken about pineapple juice. Content of fruits such as peaches, pears, and apples is low and variable; in some parts of the world, some varieties of apples have been reported to have as high as 6 or 8 mg. per 100 Gm. of apple. That might very well make an important contribution to nutrition in certain sections of the country, but some varieties of apples have practically no ascorbic acid in them, so it is not a dependable source and it is always low. The other common fruits generally are low.

DR. DRAKE.—Don't you think that some of those earlier reports on the amount of vitamin C in apples were due to errors in the titration technique?

DR. BESSEY.—They might have been, but I know of recent determinations made on several varieties of Washington apples which indicate that some varieties, at least, do contain ascorbic acid in appreciable amounts, as previously reported.

DR. DRAKE.—Out of forty varieties of apples in Ontario, we have found that thirty-nine have less than 1 mg. per cent, less than 1 mg. per a whopping big apple. In one variety, we have found, let's say, 3 or 4 milligrams. We are checking on that fortieth variety at the present time.

DR. BESSEY.—We can sum all this up by saying that other fruits do not represent the reliable source obtained in tomatoes, tomato juice, and citrus fruits.

DR. DRAKE.—How about limes?

DR. BESSEY.—Limes run definitely lower than the other citrus fruits, but they are nevertheless a potent source; the quantity of limes used, however, is not sufficient to class them as important in the same sense as oranges and grapefruit. Analysis indicates that lime juice contains about 30 mg. per 100 Gm. That would place it between tomatoes and oranges.

DR. DRAKE.—In the case of bottled lime juice, which is sold very widely in Canada, we found that you would have to drink about half a bottle of the stuff to get enough vitamin C to equal that contained in three or four oranges.

DR. BESSEY.—I'm glad that Dr. Drake made that point. I was speaking about fresh limes, of course. But that brings to mind the so-called "orange drink" sold under several brand names at lunch counters. These are reconstituted orange juice, made by adding water to a concentrated orange juice, and they contain no ascorbic acid. This is important because we have found a number of mothers who have thought that this was a cheap and easy way to give orange juice to their children. After a while they got into trouble, of course. Frozen orange juice used to be sold by some of the dairy concerns. It was a fairly satisfactory source of vitamin C. The only danger was that once in a while it thawed before it reached the consumer, and then the loss of vitamin C was considerable.

DR. H. P. LEDFORD, WICHITA FALLS, TEXAS.—Have canned citrus fruit juices been sterilized by heat as a rule?

DR. BESSEY.—Yes, the canned citrus fruit juices that are now on the market have been sterilized by heat. A few years ago, the ascorbic acid content of these canned juices was discouragingly low, but canning processes for that type of food seem to have improved the last few years. It has been our experience that most of these products run at least 75 per cent of what you'd expect from the fresh juice and much of it closer. There still may be canneries that produce a poor product, but in general, that is not true now.

DR. ALTON GOLDBLOOM, MONTREAL.—Years ago when Hess and others showed that foods could be irradiated to enhance and give them an antirachitic value, irradiated milk was shown to be more effective than cod-liver oil for the same dosage of vitamin D. Later, it was suggested that the increased effectiveness was not due to any change in the milk or a different action, but rather to a greater dispersion of it in the food. Later it was suggested that perhaps vitamin C added to, or rather dispersed in, food would have an optimal action, with a lesser quantity of vitamins. I should like to know if Dr. Bessey holds such views. For in-

stance, the chance of better absorption through wider dispersion would decrease the optimal dose as compared with when it is given all at once.

DR. BESSEY.—Most animal experiments along this line seem to indicate that this is not the case with vitamin C. Orange juice gives approximately the same antiscorbutic activity as the same amount of pure ascorbic acid, although I seem to recall some evidence from Toronto which suggests that in human beings there is something to be gained by ascorbic acid given in this form. On considering the chemistry of vitamin D and vitamin C, one would predict that dispersion would be of greater importance for vitamin D absorption. For optimum vitamin D absorption, normal fat absorption is necessary, and dispersion plays an important part in fat absorption. But with vitamin C, we have a small molecule that is water-soluble and very diffusible, and because of this, dispersion would not be a problem. In this case, considering our present limited knowledge, the answer can't be given too dogmatically either way.

DR. D. B. LEITCH, EDMONTON, ALBERTA.—Are there any other clinical disorders besides scurvy that are supposed to be due to a lack of vitamin C?

DR. BESSEY.—In the literature you can find reports that almost everything under the sun has responded to ascorbic acid, especially to high doses. We have to take most of these reports with a grain of salt at the present time. The only well-established function of ascorbic acid is its necessity for the formation of matrix materials which make up connective tissue; and of course, it's the failure of these tissues that lead to the typical picture of scurvy. However, ascorbic acid, when given in high doses, might exhibit certain pharmacologic properties not shown in the usual intake. I would say, however, that until more substantial evidence is available, we know only one function. We know that in infections, the ascorbic acid value of blood plasma and the ascorbic acid value of tissues decrease. This is not peculiar to vitamin C, however; we experience the same fluctuations with many of the other vitamins in the body fluids during infections. This has been interpreted as an indication of increased demand during infections.

As to whether high doses of this material will sidetrack a cold in the early stages, it would be very dangerous to draw conclusions about that at present. We could not recommend the use of vitamin C for stopping colds with our present information.

DR. A. P. BLOXSOM, HOUSTON, TEXAS.—A baby occasionally spits up orange juice and has a rash around the face. There is the same reaction to ascorbic acid. What would you think of this?

DR. BESSEY.—Once in a while you do find a genuine case of allergy to orange juice, but in this case, if ascorbic acid also gave the reaction, I would assume that the orange juice wasn't specific in the effect; and one would look elsewhere for the trouble; i.e., perhaps anything acid might cause this trouble.

DR. MCCUNE.—What is the allergen in orange juice?

DR. BESSEY.—There is a certain amount of protein in orange juice, and it would seem to me likely that these proteins could become allergens in the same manner as the proteins from other sources. I have the impression from what little experience I have had with food allergy that more evidence than spitting up or refusal is necessary before concluding that allergy is involved. I have seen several children who were supposed to be allergic to orange juice or milk fail to give

evidence of this on careful testing. This is especially important in the case of milk, because substitutes for milk are difficult to devise, and very often these children are not well nourished by a substitute. It seems to me that drastic changes in diet made without knowledge of the possible consequences are ill-advised.

QUESTION.—How much vitamin C is there in prune juice?

DR. BESSEY.—Prune juice, canned or otherwise, contains no ascorbic acid. I know of several cases in which the physician has taken orange juice from the child's diet, usually because he thought the child was allergic or because of gastric disturbance, and replaced it with prune juice. If this continues for long, scurvy will certainly appear. The use of pure ascorbic acid now solves many of these problems.

DR. GOLDBLOOM.—What about cabbage and Swedish turnips?

DR. BESSEY.—They are good sources of ascorbic acid. The only thing is that methods of preparation are very important in these two products. In cooking, you may destroy practically all of the vitamin C. Cabbage used in cole slaw is a good source of ascorbic acid. Turnips—Swedish turnips and turnips of all varieties—are fairly good sources, but the loss is pretty heavy in cooking, and of course, most of that material is cooked before it is consumed.

QUESTION.—What about sauerkraut?

DR. BESSEY.—Sauerkraut cannot be considered an important source of vitamin C.

DR. R. W. HOLT, NIAGARA FALLS, N. Y.—At what age must you start the child on vitamin C?

DR. BESSEY.—A normal breast-fed child starts getting from 25 to 40 mg. of ascorbic acid in breast milk within a few days after birth. This is strong evidence, I think, for an early addition to formula-fed babies. It is a rather general practice now, I understand, to start giving pure ascorbic acid to formula-fed babies after the first week. It would be good nutritional practice to gradually replace this with potent juices as the child becomes older, for the reasons previously stated.

DR. A. F. ABT, CHICAGO.—Why not give the mother of a breast-fed baby vitamin C?

DR. BESSEY.—That would be a correct procedure, since the baby would then receive it in the milk.

DR. MOSES COOPERSTOCK, MARQUETTE, MICH.—Is there any difference between requirements in children and adults?

DR. BESSEY.—Undoubtedly there is, although I am not sure that the reason is known. One can reach the maximum level in a child with 40 to 50 mg. daily, while it takes something over this for adults. Data are not available, however, to answer this question precisely.

CHAIRMAN TISDALL.—Before going on to the next item on the program, we should all keep in mind the very practical points that Dr. Bessey has brought out.

First, that the vitamin C or ascorbic acid level in the blood is no indication of the presence or absence of scurvy. He has told you that you may get an absolutely negative measurement in the blood and still the child will show no evidence of scurvy.

On the other hand, to get the highest possible level in the blood, a condition which we can say with certainty would be up to the optimum intake, he has brought out very clearly that with the older child the only way has been to see that the child gets 3 oz. of citrus fruit juices daily. That is a very striking statement. He said that most children regularly consume such a small quantity of ascorbic-acid-containing foods other than citrus fruits and tomatoes that it is necessary to see that at least 3 oz. of citrus fruits or the equivalent in tomato juice is included in the daily diet if the highest possible blood level of ascorbic acid is to be maintained.

The other point is that it requires about double or a little more than double the amount of tomatoes to produce the same effect. That's important for us as pediatricians to remember in looking after our older children.

DR. BESSEY.—I want to emphasize that what I have said meant no discredit on the foods that have low amounts of ascorbic acid in them. They form an important source of ascorbic acid for a big proportion of our population.

CHAIRMAN TISDALL.—We are all concerned not only with prevention of scurvy but with getting the maximum possible level of health in our children. The points that Dr. Bessey has brought out are most important. By taking vegetables and ordinary fruits, you will avoid scurvy in all probability, but you will not have the blood and the tissues up at the highest possible level of vitamin C unless you give 3 oz. of orange juice or an equivalent intake of vitamin C in the form of tomato juice, about 6 or 7 oz. each day. I will now ask Dr. McCune to lead the discussion on vitamin D.

DR. McCUNE.—Before starting I desire to comment on the distinction between maximum and optimum. I was much interested a few years ago to read one of Dr. Henry Sherman's early papers on the retention of dietary calcium. He studied a group of children at two levels of intake of milk, the first a pint and the second a quart. With the greater intake, increased retention of calcium was demonstrated. The feature of the paper which struck me most forcibly was the consistent reference to the increased retention as being optimal; in no case was it characterized simply as maximal. In the field of nutrition we have to be careful to distinguish between that which is better and that which is merely larger. There is evidence to suggest that accelerated rate of growth may in some instances be correlated with shortened life and may not necessarily represent a true benefit to either the individual or the community. These are general remarks and I shall terminate them at this point.

As has been shown to be true of many of the vitamins, what we used to call vitamin D has been demonstrated to be not a single entity but a complex which includes ten or twelve members. Of these, we are formally concerned with only two, vitamin D_2 and D_3. The designation, vitamin D_1, is a misnomer, having been employed for a short time by Windaus to identify a preparation which was subsequently found to be a mixture; the term is no longer used.

Vitamin D_2, or calciferol, is produced by the activation of ergosterol; it is the viosterol vitamin, the vitamin of plant origin. Vitamin D_3 results from the ac-

tivation of cholesterol and is technically known as irradiated 7-dihydrocholesterol or dimethyl-dihydrocalciferol.

These species of vitamin D appear under a good many different guises. It is not necessary to describe in detail the forms and vehicles in which they are procurable. You know, for example, the methods by which milk can be fortified. This may be done by irradiation; in this case the cholesterol of the milk is activated and animal vitamin D, vitamin D_3, results. If irradiated yeast is fed to the cow, the vegetable form, D_2, appears in the milk. Concentrates of either animal or vegetable origin can be added directly to the milk before bottling. Until recently it has not been possible to irradiate milk to a potency of much more than 150 U.S.P. units per quart without imparting to it an unpleasant taste. This obstacle has been surmounted.

Since the volume of a given preparation of vitamin D supplies no information concerning biologic potency, it is important to regulate dosage and to calculate cost on the basis of a standard of comparison. The older rat unit has been replaced by the U.S.P. or international unit; 0.025 mg. of calciferol equals 1 unit.

Perhaps the best way to approach a discussion of the clinical uses of vitamin D is to ask the question, What can the vitamin be expected to accomplish? Its most familiar function and that which still serves as the basis for the standardization of all preparations is the capacity of vitamin D to prevent and cure rickets. It is obviously not comprehensive to appraise the total biologic value of vitamin D on the basis of this single capacity. The muscular weakness which characterizes severe rickets may be adduced as an example of another manifestation of the result of privation of vitamin D, more specifically of its influence on the metabolism of phosphorus. The occasionally alleged ability of vitamin D to prevent infection can be disposed of briefly. Individuals suffering from serious privation are more susceptible to infection than others; however, it has never been shown that the vitamin possesses specific value in this respect.

You have heard a good deal in the last three or four years concerning the use of heroic doses of vitamin D in the treatment of rheumatoid arthritis. In lack of personal experience, I hesitate to express an opinion on this point. The published reports claiming success are not convincing. The only study that I am aware of in which crystalline vitamin D_3, calciferol, was used in the treatment of arthritis led to substantially negative results. The treatment of psoriasis with large doses of vitamin D has not been proved to be dependable.

The use of single massive doses of vitamin D in the treatment of rickets and tetany appears to have acquired popularity in Germany, where it was introduced in Harnapp, but it has not been widely practiced in this country. The method—*Stosstherapie*, as it is called—consists in the administration of 10 to 15 mg. (400,000 to 600,000 U.S.P. units) as a single dose either orally or intramuscularly; the latter route obviates danger or failure of resorption. This therapeutic technique may be borne in mind for special situations, but no general need of it exists in this country. For us, its greatest utility is realized in those increasingly rare instances where severe rickets is complicated by pneumonia and where rapid cure is desirable. The method also recommends itself in situations where lack of maternal cooperation makes it desirable to administer treatment in the physician's office. It can also be used prophylactically under the same circumstances.

Extensive studies in Europe have failed to demonstrate that the method is harmful. However, the fact that the indiscriminate use of vitamin D is capable of producing poisoning makes one reluctant to urge the widespread use of massive single doses, either prophylactically or therapeutically. Although it is probable that the cases of vitamin D intoxication that came to light in conjunction with the early use of the crude German preparation, vigantol, were due to by-products

of irradiation, it has been shown with virtually pure preparations that crystalline vitamin D itself can be poisonous in large doses. The symptoms represent a magnification of the familiar biologic effects of vitamin D, namely, conspicuous elevation of the serum calcium, sometimes amounting to 18 to 20 mg. per 100 c.c., and rise of serum inorganic phosphorus. Marked hypercalciuria and hyperphosphaturia occur; the urine contains large amounts of amorphous sediment as well as casts composed of basic calcium phosphate. We have had an opportunity to study the initial manifestations of vitamin D poisoning in conjunction with the treatment of three cases of refractory rickets in which the disease could be controlled only by the administration of approximately 100,000 U.S.P. units of vitamin D daily over long periods of time.

The treatment of hypocalcemic tetany in infants and adults has been improved by the development of *Stosstherapie*, best employed in conjunction with supplementary administration of ammonium or calcium chloride, and also by the introduction of dihydrotachysterol, otherwise known as A.T.10. This substance is structurally related to vitamin D. Its mode of action is qualitatively similar to that of vitamin D, but, according to Albright, differs from vitamin D in that it disproportionately accelerates the absorption of calcium from the alimentary tract and the excretion of phosphorus by the kidneys.

DR. DRAKE.—Could you tell us something about the relative efficacy in a human being of vitamin D_2 and D_3?

DR. McCUNE.—There has been a great deal of controversy on that point. It arose when the observation was made that vitamin D_2, viosterol, was only about one one-hundredth as effective as cod-liver oil in the prevention and cure of rickets in chickens. This started a good many people inquiring into the matter. Without going into detail, it is fair to say that they are both thought to exhibit almost equal biologic potency in man.

DR. R. E. PRAY, FARGO, N. D.—What is the danger in the combined use of cod-liver oil and calcium? We hear about the danger of giving calcium and vitamin D and bringing about changes in the body.

DR. McCUNE.—I don't know the full extent of those dangers. I have quoted many times Dr. Ross' report to the American Pediatric Society last year of four cases of vitamin D poisoning in infants who, through misunderstanding, received between 20,000 and 40,000 units daily over a considerable period of time. Under these circumstances, fatal vitamin D poisoning developed in two cases; occurrence of metastatic calcinosis was demonstrated at autopsy in one case.

There is no danger of injury with doses under, say, 3,000 units daily whether or not moderate amounts of calcium are given in addition. It must be stated that we know nothing about this in terms of long-time follow-up—whether the incidence of arteriosclerosis at 72 is increased by the generous administration of vitamin D during infancy, childhood, maturity, or late life. There is no particular reason to anticipate that danger if you stay within the ordinary limits that we employ.

DR. G. L. HACKER, DALLAS.—What are the vitamin D requirements in the prepuberty period, the rapid growth period, when there is supposed to be a negative nitrogen-calcium balance?

DR. McCUNE.—Four or five hundred units would cover it pretty well. This estimate is tentative.

DR. HACKER.—Should they be given extra cod-liver oil at that time?

DR. McCUNE.—I'm not entitled to express an opinion based on personal experience, but I think it reasonable to say yes.

DR. W. R. SISSON, BOSTON.—Should infants with craniotabes be treated with vitamin D?

DR. DRAKE.—Some cases of craniotabes are caused by a localized osteoporosis, due perhaps to withdrawal of calcium from the skull bones or laying down at the end of the long bones, but every case of craniotabes is not rickets.

DR. McCUNE.—I once had an interesting pair of monozygotic male twins. Both received identical amounts of vitamin D of the same source and took it equally well. One twin, for reasons that I can't at the moment remember, was somewhat more aggressive than the other in getting around and not remaining in one position, whereas the other lay more or less consistently on one side; he developed conspicuous craniotabes whereas the other did not. I might specify in addition that the rate of growth of the circumference of the two heads was identical. It was clearly a pressure phenomenon. Clinical experience has further demonstrated the occurrence of a type of craniotabes that cannot be rapidly rectified by vitamin D. Pressure atrophy, or, if you like, pressure aplasia, explains the origin of a good many examples of craniotabes.

DR. ABT.—I can tell from the way you placed your hand that this was unilateral.

DR. McCUNE.—In the case I spoke of, the softening was unilateral.

DR. ABT.—Most rachitic craniotabes is bilateral.

DR. McCUNE.—Not necessarily. I think the factor of pressure operates to intensify the symptom even when it is rachitic in origin. No?

DR. ABT.—I can't remember. All the cases of craniotabes I've ever felt definitely associated with rickets were bilateral as far as I could determine.

DR. McCUNE.—Bilateral, but not bilaterally symmetrical in all cases.

DR. J. L. STOKES, PHILADELPHIA.—How much variation do you think there is between different infants? Dr. Rappaport has carried out a longitudinal study for one year. On one group of infants receiving 135 and another group receiving 1,200 units of vitamin D. The two groups showed no bone differences as the subjects increased in age. One explanation for that might be the fact that a certain number would always require . . . anyway, the majority would get along perfectly well on 135 units. I think there may have been overemphasis on the exact requirement of 400 to 600 or 800 units. A moderate amount will satisfy the vast majority if a physician could be allowed to determine the amounts beyond that.

DR. McCUNE.—I think that is eminently true, and that is the reason I estimate dosage from the point of view of public health. A smaller dosage than is usually given is probably adequate, but I don't suppose we will ever, at least not soon, persuade the practitioner to depend uniformly on the smaller dosage and I am not really sure that we should try because the patient can afford the extra unitage.

It apparently does no harm.

In attempting to explain some of the variability of the incidence of rickets in the same population, I would like to mention Dr. Shohl's most interesting work concerning the level of intake of minerals other than calcium and phosphorus, the acid-base balance of the diet, and the presence in the diet of certain organic anions which, in conjunction with cations, yield a buffer system. Dr. Shohl showed experimentally in animals that a mixture of citric acid—sodium citrate or a mixture of tartaric acid—sodium tartrate was quite effective in the prevention and cure of experimental rickets. He and Butler published two cases in which cure of infantile rickets was attained by the use of these mixtures. I don't know that the citric acid content of milk is of great importance, but it seems to me that these experiments illustrate possible causes of the variation in the incidence of rickets.

I have not seen a good study on the correlation between rate of growth and the appearance of rickets. We all talk about it, but I haven't seen a mathematical treatment of the matter.

DR. LEITCH.—Can the quantity of milk one drinks be overdone with regard to utilization of calcium?

DR. McCUNE.—It is not apt to be overdone from the point of view of the utilization of calcium. However, around New York where the quart-of-milk doctrine was preached vehemently for many years, we do encounter feeding difficulties, largely of psychologic nature based on the attitude of the mother that the quart of milk must go in every day whether school keeps or not. For that reason, I think we all are inclined to take issue with those who insist on the daily quart of milk.

DR. GOLDBLOOM.—Perhaps it's worth pointing out, parenthetically, and this is important to the Canadian members, the extra harm that this quart-of-milk preaching has done in Canada, because our quart is 40 oz.

DR. McCUNE.—I am personally persuaded that the ideal way to get vitamin D in is to include it in milk of sufficient potency so that you are assured of adequate protection.

I would be in favor of the idea of milk's being uniformly fortified to a potency somewhat greater than that attained by irradiation because of what Dr. Stokes and I have discussed, namely, the insecurity concerning the adequacy of 150 units. When it comes to the use of concentrates, I think those which contain a good deal of vitamin A should be preferred to those that contain D alone, unless there be some special indication to the contrary.

CHAIRMAN TISDALL.—The next on the program is Dr. Drake who will lead the discussion on vitamin K.

DR. DRAKE.—Our first lead regarding vitamin K was around 1928, when Dam found that chickens which he had on a special diet for the study of sterols developed skin and muscular hemorrhages. Later on, he found that the addition of cabbage to this particular diet would prevent the development of these hemorrhages. A little later he found that none of the known vitamins, including vitamin C, would prevent this hemorrhagic condition and hence the name of K was given to this particular vitamin from "Koagulation."

Vitamin K is found naturally in green and leafy plants. It is fat-soluble, stable to heat, destroyed by light, and destroyed in alkaline solutions. Since that time,

vitamin K has been prepared in pure form and various substances which have a vitamin K-like action have been synthesized.

Probably in the future, rather than using the original vitamin K, either natural or synthetic, we will use one of these vitamin K-like substances, because they can be prepared much more cheaply than the original vitamin K, either K_1 or K_2. Vitamin K is necessary for prothrombin formation, prothrombin being prepared in the liver. K must be absorbed to be available for prothrombin formation. Remember that up to the present, most of the K preparations are in oily solutions, and hence where there is any biliary obstruction, with absence of bile salts in the intestine, bile salts must also be given by mouth with the oily solutions of vitamin K to obtain absorption.

At the present time, a number of the drug houses have in the experimental stage water-soluble K preparations which will probably be valuable in more conditions than are the oil-soluble K preparations. Vitamin K is of value only in conditions where hemorrhage is due to a decrease in prothrombin. It is not valuable in purpuras or in hemophilias; it is valuable in hemorrhages which are the result of a lowered amount of prothrombin, such as those which occur in biliary stenosis, biliary fistula, and in hemorrhagic disease of the newborn infant.

In the cases where there is deficiency of bile salts in the intestinal tract, bile salts must be administered, if you are using a vitamin K which is soluble in oil. Let us first take up the question of prophylaxis in hemorrhagic disease of the newborn. The work that I am going to tell you about was done by Dr. Snelling in Toronto. He observed a large group of pregnant women taken from the outpatient class of one of our hospitals. Half of them were receiving 1 mg. of vitamin K by mouth per day and half the group were without the addition of this substance. He estimated the prothrombin time in the cord blood of the infants borne by these women. An increased prothrombin time is evidence of a decreased amount of prothrombin in normal individuals. Using Quick's method, he found in normal individuals a range of somewhere from fifteen to thirty-five seconds as the prothrombin time, the length of time that it takes for a clot to develop under certain conditions, using the blood of the patient under observation. He found in the first place that in practically every case there was less prothrombin in the cord blood than there was in the mother's blood. In the group of children born of mothers who were not receiving this 1 mg. of vitamin K per day, the cord blood prothrombin time ranged from about thirty seconds to more than one hundred and twenty seconds.

In the offspring of the mothers who were receiving vitamin K, the prothrombin time was lower than this. None was more than ninety seconds. This vitamin K was given by mouth, and the mothers were asked to take vitamin K, 1 mg. per day, for one week before the expected date of confinement. It worked out that these mothers received a daily dose of K for from two to sixteen days before confinement. Apparently, two days is long enough to administer it, if one is absolutely sure that he can begin just two days before confinement. There was no difference in the prothrombin time of infants born in this two-day group and those born in the sixteen-day group.

Now one point that I would like you to remember is that a large number, let's say about 15 per cent. of the infants born of the mothers not receiving vitamin K had a prothrombin time greater than one hundred and twenty seconds.

Dr. Snelling next went to work to study the prothrombin time in infants suffering from hemorrhagic disease of the newborn. Their prothrombin time was from one hundred and sixty-seven seconds up to infinity, no clot formation at all. But remember that a certain number of the infants born of mothers not receiving

K had prothrombin times as long as the infants actually suffering from hemorrhagic disease of the newborn, but they did not bleed. There is some other factor in hemorrhagic disease of the newborn besides a decrease in prothrombin.

In the treatment of these cases of hemorrhagic disease of the newborn, Dr. Snelling first administered vitamin K by mouth. In one case, he found that he could cure the hemorrhagic disease in four hours by administering 1 mg. of K. Of course, there is always the danger that you may not get the effect of the vitamin K because of nonretention, so in the treatment of hemorrhagic disease of the newborn, we would prefer to use some solution of vitamin K which could be administered parenterally.

In the treatment of hemorrhagic disease of the newborn, in about nine consecutive cases, through the injection of 1 mg. of vitamin K intravenously, Dr. Snelling has cured the hemorrhage in four hours or less. Our previous treatment of hemorrhagic disease of the newborn was by means of blood transfusion, but we have found in the past that 20 per cent of all our cases of hemorrhagic disease of the newborn treated by transfusion alone required more than one transfusion to stop the blood loss. We would suggest that the treatment of hemorrhagic disease of the newborn be the injection of vitamin K, 1 mg. intravenously or intramuscularly. Before you inject the vitamin K, make a hemoglobin determination on the infant and see whether the loss of blood has been so great that that should also be repaired. Where there has been a large loss of blood, inject not only the vitamin K, but also give a transfusion of blood.

DR. SISSON.—Will you tell us something about the importance or lack of importance in giving vitamin K to premature infants?

DR. DRAKE.—One is more likely to find bleeding in premature infants than in full-term infants. In a higher percentage of premature infants the prothrombin time is going to be in the range where hemorrhagic disease of the newborn occurs, and they should all receive it prophylactically.

DR. COOPERSTOCK.—Isn't vitamin K given parenterally to mothers at the beginning of labor effective too?

DR. DRAKE.—Yes, but the price of this vitamin K capsule is very low; you can get them commercially for two or three cents each and I think I would give the mother a few vitamin K tablets at a cost of, say, fourteen cents than go to work and administer a parenternal injection.

DR. ABT.—Did you investigate the dietary habits of this group of mothers who received no vitamin K, to see if there was any reason why there should be such a prolonged prothrombin time?

DR. DRAKE.—No, for there was quite a large group. There were about a hundred in each group, the same class of population and at the same time. Alternate cases were put on one side or the other side of the observation, but we did not check their dietary carefully. I think the good diets would be about equally divided between the two sides of the group.

DR. HEARN BRADLEY, NASHVILLE.—What is the value of vitamin K in rather severe deliveries to babies who have petechial hemorrhages, not single large hemorrhages, just the oozing type, that will keep glued and cause symptoms later.

DR. DRAKE.—Vitamin K will be absolutely useless in any condition where you do not have a lowered amount of prothrombin as evidenced by a long prothrombin time.

DR. BRADLEY.—You wouldn't give it as a prophylactic measure to these babies?

DR. DRAKE.—I would give it to every woman in an attempt to get the prothrombin time down, and if you have not given it, quite a few of the infants are going to have prothrombin time in the range where hemorrhagic disease of the newborn occurs; but in any given case at the time of bleeding, if the prothrombin time isn't increased, that is, if the amount of prothrombin is down while the infant is bleeding, vitamin K is not going to be useful.

DR. L. H. MUSE, ATLANTA.—Has there been any trouble from the intravenous injection?

DR. DRAKE.—No, we have not run into any difficulties at all, and one certainly has a wide range of safety. You could administer a thousand times the normal dose without running into any toxic effects.

DR. P. E. LUECKE, DALLAS.—In the case of premature infants, of course, where delivery comes on before the expected time and the oral administration can't be used, what would you specify as the amount of vitamin K to be given at the onset of labor to produce the desired effect in the offspring. How rapidly does it act through the mother on the child?

DR. DRAKE.—I can't answer that question. We are working at the present time on administering vitamin K by mouth to pregnant women when first seen after the onset of labor, and we haven't our results yet. In the case of premature infants, I would probably give vitamin K by mouth to the infant, let's say 1 mg., and another dose in twenty-four hours.

DR. BRADLEY.—The prothrombin time of infants is known to be longer twenty-four hours after birth than it is at 4 days of age.

DR. DRAKE.—There you get into the question of the fact that vitamin K is synthesized by the intestinal bacteria. At twenty-four hours the bowel has not yet been infected by the bacteria which will synthetize vitamin K.

CHAIRMAN TISDALL.—Dr. Drake has brought out some very important points. One we all should recognize—that many of these normal infants have prolonged prothrombin time, a prothrombin time in the range which is always found with hemorrhagic disease of the newborn, which, as he has pointed out, would indicate that those may be potential hemorrhagic cases. With a certain degree of injury, the infant may then start to bleed. One of the things we may want to do as a routine is to give some vitamin K to the mother before labor and possibly as well to the youngster after birth.

CHAIRMAN TISDALL.—The next speaker on the program today is Dr. Sebrell of Washington, who is going to deal with the whole group of the vitamins coming from the vitamin B complex. In addition to that, he is going to take a little time to bring your attention the importance of proper nutrition from the national standpoint. This is a view in which I think we, as pediatricians, should take a very leading part, when we realize that the diet here in the United States contains

many foods which are completely lacking in minerals and vitamins. For instance, our Canadian figures show that the average intake per day of white flour furnishes roughly 700 calories; sugar, around 500; molasses, around 42. A total of about 1,300 calories, or roughly 50 per cent of the total calorie intake, comes from foods which are completely devoid and lacking, or very low, in minerals and vitamins.

If we add to that glucose, corn syrup, and certain processed fats, you find that the whole load, the whole load for the supply of vitamin and minerals in the American and Canadian diet, falls on just one-third of the caloric intake. Now think of that! Think of the importance of that from a national standpoint. There is lots of evidence, as Dr. Sebrell will bring out of the fact that when these substances are very low it interferes with the efficiency of the nation as a whole. We in Canada, of course, are greatly interested in that particular thing at the present time. Great Britain has taken active steps to do something about it, adding vitamin B_1 to flour. In 1941, all flour sold in Great Britain, as soon as they can arrange it, is going to contain vitamin B_1. You can see the possible significance of this. Just one-third of the national diet, caloric intake, has to supply all of the minerals and vitamins, and that's the result of the modern processing of food.

White flour was only introduced in 1880. Sugar was introduced one hundred years ago, and the average intake was around 9 pounds per year; now it is over 110 in the United States and 100 in Canada. So you see what a great national problem this is, and there is no person who knows more about it than Dr. Sebrell. He is going to take a little time after he has discussed vitamin B from the standpoint of its pathology and the symptoms and so on, to deal with this national question. When the point does come up, I think that we, as pediatricians, should be the leaders in our communities to see that effective support is given to Washington and to Ottawa in everything that can be done to improve the nutrition of the nation.

DR. SEBRELL.—The deficiencies in the vitamin B complex in this country are the most widespread and most serious deficiency diseases that we have at the present time. That is a point of view which is quite different from the one existing just a few years ago when we felt that beriberi was a tropical disease and pellagra was of interest only in the southern United States. We now think that both of these diseases in mild form or in forms which were hitherto unrecognized exist all over this country.

The vitamin B complex consists of an unknown number of substances. There are five substances which have been definitely identified and are now synthetically prepared and available. Of those five at the present time, only three are known to be of much clinical importance. They are thiamin, riboflavin, and nicotinic acid. The two which appear to be of less importance today are pyridoxine, which was formerly called vitamin B_6, and pantothenic acid.

Those two substances have undergone much laboratory experimentation, and I might mention briefly some of the laboratory findings just so that some of you may see some clinical application for these things, because many of us feel that it would be most unusual if the human organism did not require them in some way. Pantothenic acid deficiency in rats causes a hemorrhagic necrosis of the adrenal glands; that is the lesion of principal significance. It also causes graying of the hair in black rats, but I do not believe it is of any value in treating human graying of the hair.

Pyridoxine deficiency causes a condition in rats which has been called rat acrodynia and is characterized principally by swelling, redness, and scaliness of the paws and also of the ears; it was formerly called rat pellagra by some investigators.

Dr. T. D. Spies and his associates see some evidences of pyridoxine deficiency in human beings. The symptoms unfortunately are vague, and the diagnosis is on

such symptoms as weakness and some difficulty in walking. However, these patients do better when he gives them pyridoxine, and he has been able to demonstrate in them a decreased excretion of pyrodoxine in the urine before he treats them. Pyrodoxine deficiency in dogs causes an anemia; in human beings, apparently it is of no value in any of the anemias in which it has been tried.

The other three vitamin deficiencies are more serious. Frank beriberi or tropical beriberi is not so very common, but the symptoms of a lesser degree of deficiency of thiamin are very widespread. The work of Wilder and his associates at Rochester was published just last October on a group of women who were experimentally studied on diets of restricted thiamin content. These women showed loss of appetite, fear complexes, and had the symptoms of what would be called a neurosis. Soma Weiss in Boston has studied the heart changes in a number of people with thiamin deficiency, and Jolliffe in New York has made similar observations. They believe that heart changes as characterized by conduction changes, that is, inversion to the T wave, are symptoms of early thiamin deficiency.

So there is good reason to believe that we have a considerable amount of thiamin deficiency in this country, and from the point of view of children, it is important to recognize that in the experience with tropical beriberi, it has been found that the breast-fed infant may have beriberi although the mother may show no severe symptoms of the disease.

The second member of the group, riboflavin, has been recognized to be of clinical importance only within the past two years. A deficiency in riboflavin is characterized by erosions at the angles of the mouth, reddening, denuding of the lips, which has been called a cheilosis, a purplish-red discoloration of the tongue, which becomes magenta color, with flattened papillae, and a growth of capillaries into the cornea, causing an interstitial keratitis.

I think that perhaps some of the cases that were called perlèche could easily have been caused by riboflavin deficiency.

The third member of the group is nicotinic acid, deficiency of which characteristically, as you know, causes pellagra. In addition to the typical skin lesions of pellagra, however, there has been recent evidence to indicate that nicotinic acid deficiency may manifest itself without the typical skin lesions. Both Jolliffe and Sidenstricker and their associates have reported mental changes in patients, which Jolliffe has called encephalopathy. The patients are confused and disoriented, having symptoms similar to those of cerebral arteriosclerosis, but which respond rapidly to very large doses of nicotinic acid.

They regard these cases as being acute nicotinic acid deficiencies. Now I might call your attention to one of the facts about pellagra which has been frequently overlooked. In the old surveys of the incidence of pellagra in the United States which were conducted by Goldberger in mill villages in South Carolina, in which house-to-house canvasses were made and all the cases of pellagra in those villages were seen, the largest number of cases was found in the age group of between 12 and 15 years. Those cases had been entirely missed in the statistics on pellagra because the patients never got to the hospital. Those children were found playing around and going to school with the skin lesions of pellagra on them. The disease seemed to be a mild one which didn't require hospitalization and therefore was not picked up.

So it is possible, according to those data, to regard pellagra as primarily a disease of childhood. This is because the children in the lower economic groups, after they get a little older, don't get any milk; they aren't old enough to work and therefore can't supplement their diet outside of the household, and they are most likely to get a deficient diet.

Now in clinical experience, the above three diseases do not occur separately. It's the rule rather than the exception to find symptoms of two or all three of them in the same individual at the same time, because the foods which contain one of the vitamins usually contain the others to some extent, and if the diet is such that it is deficient enough in one to produce the symptoms of that condition, it is likely that the symptoms of one of the other two diseases also will be present. However, if not present, they may appear while the patient is being treated with one of the pure vitamins.

We have seen patients with pellagra, while being treated with nicotinic acid, develop riboflavin deficiency symptoms in the hospital while they were under treatment. We have seen patients with what appeared to be pure riboflavin deficiency treated with riboflavin and maintained on a deficient diet who developed symptoms of pellagra; also we have seen patients with pellagra being treated with nicotinic acid and developing symptoms of beriberi.

In clinical practice, unless you are sure of the diagnosis and that the patient has only one of the diseases, it is safer to use a mixture potent in all three of these substances, in order to be sure that you clear up the condition.

These things are common, as I have indicated, and there is a paper in the *American Journal of the Medical Sciences* for November, 1940, by Dr. Spies, giving his experience with riboflavin deficiency at Birmingham where he has seen more than two hundred cases, I believe, in children. He believes that it is the commonest deficiency around Birmingham. So all three of these deficiencies are really of great clinical importance. In treatment with riboflavin, a dose on the order of 4 to 6 milligrams a day is suggested, and in some cases it may be necessary to go up to 10 mg. a day. The average daily human requirement for an adult, we believe to be in the vicinity of 2 mg. a day; that's for prevention, not for therapy.

With nicotinic acid, the dosage has varied considerably from as little as 50 to 60 mg. a day to 1 Gm. or more a day. Doses of 1 Gm. a day are really excessive, and even for unusual conditions ordinarily 300 or 500 mg. a day would be sufficient. In the case of thiamin deficiency it requires a long time for recovery to take place despite active treatment.

DR. HACKER.—Will you discuss further the requirements for infants and young children?

DR. SEBRELL.—I didn't go into the requirements of an infant more fully because we don't know too much about it. Actually there are few studies on the requirements for infants. In the case of riboflavin, the infant requirement is probably in the region of 0.5 mg. a day, and I'm basing that, not on any direct observations, but rather on the flavin content of milk which is a variable quantity, and on the assumption that a child getting a quart of milk does not ordinarily develop the symptoms of flavin deficiency; it would be reasonable to suppose that the flavin content of a quart of milk would be somewhere around an infant's requirement. That is not good evidence at all, but it is the best I can do at the present time.

We don't know the nicotinic acid requirement for either children or adults. I have been trying for two years to determine experimentally the human nicotinic acid requirement. It's a difficult problem for several reasons. The urinary excretion decreases a little, but there is still a lot there, and that is complicated by the fact that you get several nicotinic acid combinations or related compounds, metabolic products of nicotinic acid, and related substances in the urine which very greatly complicate the tests. Being handicapped in these two ways, it has

been very difficult to arrive at any guess even as to what the human nicotinic acid requirement is. There just isn't any figure.

DR. HACKER.—I usually add the vitamin B complex at 2 months of age in very small doses, to carry the infant until he starts on solid foods.

DR. SEBRELL.—An infant getting milk and cereal, egg and vegetables, is going to get plenty of this group. Incidentally, in treatment, you don't have to worry about toxicity here. With all three of these no one has demonstrated any toxic effects from enormous dosage. The excess appears to be excreted, and we have seen no damage of any kind from tremendous doses.

DR. R. L. NELSON, WICHITA FALLS, TEXAS.—How long would it take to expect a response in the lesions?

DR. SEBRELL.—We can see improvement in forty-eight hours. Of course, the lesion is not healed, but we can see the lesion is changed in appearance so that it has the appearance of a healing lesion within forty-eight hours. It may require from ten days to two or three months to completely heal the lesions.

DR. NELSON.—Two weeks' dosage would prove or disprove the diagnosis.

DR. SEBRELL.—Two weeks of adequate dosage would enable you to see enough change so that you would know that it was doing some good. In that length of time, most of those symptoms would be entirely gone. When I say "entirely gone," I mean that upon the closest observation we can see no evidence of any remaining lesion at all and that's when we say they are entirely gone; but in the meantime, they will clear up to where there is practically nothing left.

DR. DRAKE.—Would you mind telling the audience your observations concerning deficiencies of this group at the present?

DR. SEBRELL.—Dr. Drake is referring to a remark which I happened to make some time ago and which isn't original with me. Dr. Goldberger and Dr. Wheeler used to see the same thing and called my attention to it. I spent quite a lot of time going through the South trying to find cases of pellagra, just going up country roads and stopping at the houses, and asking if anybody in the neighborhood knew anyone who had pellagra. I can always find them; there are plenty of them during the pellagra season. The remark to which Dr. Drake refers is this: I learned very early that there is no use to stop at a tenant farmer's house to look for pellagra if you see a vegetable garden growing outside the house. Because if he has a vegetable garden, he is not going to have pellagra in his family.

That bears out the experimental observation that the green vegetables—turnip greens, mustard greens, kale, tomatoes, green peas—have pellagra-preventive value. So now, if I see some chickens and a pig or two and a vegetable garden, I keep right on going.

DR. BRADLEY.—Is there any growth promoting value to the vitamin B complex?

DR. SEBRELL.—Just as with all of the vitamins, with experimental animals a deficiency in any one of them stops growth. Dr. Spies, in the paper to which I have already referred, states that he sees a rapid increase in growth in riboflavin-deficient children when he gives them riboflavin. It is quite probable that a child with a deficiency of any one of these three, or all of them, would be underweight; and proper treatment would cause a gain in weight.

DR. DRAKE.—We have recently been doing some Vitamin B_1 and riboflavin estimations on the mothers' milk in Toronto and found that there were very wide variations in the content of these two vitamins. You could bring up the content very rapidly with administration of these vitamins. That was so in the case of riboflavin. The amount in mothers' milk is only one-tenth the value in cow's milk, even in mothers who are receiving a very good diet.

I think there might be quite a fair chance that in breast-fed infants with a mother on a poor diet you might have a deficiency in some of those substances.

DR. SEBRELL.—That would certainly be a good field for investigation and one on which we need more information.

Since we have this widespread condition of various deficiencies in this country, it seems indicated that we should do something about it in order to try to improve conditions. As Dr. Tisdall has pointed out to you very briefly, the increase in white flour consumption and the increase in sugar consumption has replaced, or displaced I should say, a fair proportion of the vitamin B complex from the American diet as it existed fifty or seventy-five years ago, and studies by Cowgill and Jolliffe indicate that the thiamin content of our diet is less today than it was at that time.

We have tried educational campaigns, and we recognize that they just don't solve the problem. We have tried the theory of raising food at home, especially in the South, and I think considerable progress has been made. I am convinced that if the people in the rural sections of the South would produce their own food supply, much of the deficiency disease in that section of the country would disappear; and as long as the price of cotton stays down, I think we can see a progress in that direction. However, I am very much afraid that if the price of cotton rises, all the gardens are going to be plowed up again.

However, that doesn't meet the problem in the cities, and it seems logical to try something other than an educational campaign. As recently as a year ago, I was opposed to the idea of fortifying foods or restoring foods, if you will, with vitamins and minerals, because I felt that the thing to do was to promote the consumption of an adequate diet, that we ought to get our vitamins and minerals from natural foods. They are there; that's the cheapest way to get them, and we should be able to do it. I am now convinced that we are not going to solve the problem practically that way. We've tried for a long time to promote the consumption of so-called whole-wheat bread, or graham flour, and we get nowhere. Most of the flour consumed in this country is still of the white variety.

Therefore, we are making efforts to secure a vitamin and mineral fortified flour of sufficient thiamin, nicotinic acid, riboflavin, and iron content to be material value in improving the diet, so that we can still have our nice, white flour, and yet painlessly get the minerals and vitamins we need. At the same time, it is important, I believe, that these preparations not contain enough to enable them to be promoted as therapeutic agents.

It is important not only to have a minimum but also a maximum level, and that point is being recognized too. I think you will see on the market within the next six months a vitaminized flour which will contain thiamin, nicotinic acid, riboflavin, and iron, and, as optional ingredients, vitamin D and calcium.

The question of sugar is another important item. Cane sugar be fortified? If so, how much should be permitted. Sugar at the present time cannot be fortified because the vitamin crystals won't stick to the sucrose crystals. A large sugar refinery, however, is attempting to develop a new method for vitaminizing sugar. If this turns out to be practical, it offers a method of getting more thiamin into the diet. Now this whole problem is, of course, intimately related to national

defense, and you will, I believe, see in the near future an active campaign to improve nutrition in this country. You as pediatricians have always led in the field of nutrition, and I think it is right and proper that you should have a leading part in any national movement to improve our nutrition.

DR. BESSEY.—The time allotted to this study is up, and it has been a most interesting discussion of vitamins. I want to say, in speaking for those people who participated, that it has been most enjoyable to us, and especially do I want to speak for myself, as a nonpediatrician, to say that we people in the experimental fields feel happy and honored to be able to help in any way that we can pediatrics and medicine in general.

PEDIATRICS AND NATIONAL DEFENSE

So much interest has been aroused in the question of pediatrics and national defense that the JOURNAL reprints excerpts from two talks which it is thought will be of interest to Academy members.

At a meeting of Region I held in New Haven, Conn., on March 27, 1941, a "smoker" evening was given over to a discussion of defense problems. Dr. Martha Eliot spoke of her recent trip to England, from which she had returned ten days before the meeting, and told of what she had seen there. Excerpts from stenographic notes of her talk have been obtained. These are followed by remarks by Dr. Wall and Dr. Stimson who discussed the talks given by Dr. Eliot, and a paper by Dr. Fred Tisdall.

In addition is a radio talk by Dr. Philip M. Stimson, Chairman of the Academy Committee on National Defense, given in Memphis at the time of the annual meeting last November. Although it is the general feeling that pediatricians are probably more valuable in looking after the civilian population in case of war than serving as army officers, there is one exception to this general rule. Pediatricians are better prepared and qualified to diagnose and treat the communicable contagious diseases than any other group of physicians.

Pediatrics in the Defense Program

DR. MARTHA M. ELIOT.—I have been to England, leaving here on January 18 with a government commission to study various phases of civil defense. The commission was made up of a representative of the War Department, Major Rydings, whose job it was to study the various aspects of civil defense more closely related to the military and police activities, such as the A. R. P., the warden service, fire protection, and so on; a representative from the Public Health Service, Dr. Parran, whose primary object was to study the emergency medical services and the public health aspects of civil defense. A representative from the Social Security Board, Mr. Jeffrey May, was there for the purpose of studying public assistance, public administration, and the various problems related to the care of people in bombed-out families, bombed-out houses, together with the problem of the care of the homeless and certain problems related to the social insurances. Mr. Fred Horner from the National Defense Commission was our expert in transportation, to study all phases of transportation in relation to civil defense. Lastly, it was decided, about seventy-two hours before the commission sailed, that perhaps, after all, problems of children were worthy of consideration, and the Children's Bureau was asked to send a representative, and I was sent.

Dr. Parran and I went first to the Ministry of Health, because naturally many of our interests centered there, Dr. Parran's interest in the general medical services and mine in child health and child welfare services. In addition to trying to get information on the care of children, I also made an effort to get as much information as possible with respect to the voluntary services in England, especially the voluntary services rendered by women in the civil defense program.

There were two major areas of interest for me. One was what was happening in cities under bombardment, before and after bombardment; and the other, what was happening to the evacuated children, whom we all know had been moved out of the cities.

The questions that have been asked me most frequently since I came home are, "What about the children? How are they? What about the morale among chil-

dren?'' From the point of view of their physical health, on the whole they are doing very well. The children in the big cities that have been bombed are naturally suffering from the effects of the bombardment, not so much in their physical health but their general emotional state. But by and large the children have stood up under it extraordinarily well. When I arrived in London the story I heard everywhere was, ''The children take this wonderfully. They take it better than anyone else.'' But gradually I found that, although that was true in general, there are a certain number of children who are disturbed by the exceedingly strenuous life through which they are being put. Not only is it a matter of having to go through the bombardments, but it is a matter of life in the shelters, a disturbed existence between their homes and the shelters, and an attempt to go to school, if they are school children, and back again to the home and then to the shelter, with meals upset and food arrangements disturbed. All this must, in the long run, have an effect upon children.

Everybody in England is on rations. Children are given priority for milk; they are to be given some priority for oranges. But there are so few oranges anyway that it is going to make relatively little difference. In visiting a number of residential nursery homes, I always made the inquiry as to whether they had a really adequate supply of oranges or orange juice for the children, and I found that practically none had. The rations otherwise are not so severe that the diet is below a minimum on which the children can continue to grow. Milk is obtained through the schools and through the child welfare stations.

The question of the emotional disturbance in children should not be exaggerated, but there is some of it. Physicians, for instance, told me that after severe bombing a few children will be brought into the hospitals, not injured physically, but disturbed emotionally. And when you think how many children are subject to this severe bombing, it is really surprising that there are not more.

In the cities under bombardment, one might have expected epidemics, but it has been extraordinary how throughout this winter there has been no serious epidemic among the population or among the children. It has been a measles year and there has been a good deal of measles, but apparently little pneumonia was associated with it.

One of the first things I did, on going into London, was to visit the child guidance clinics, or rather the workers in them, so as to get a firsthand impression of what was happening from an emotional point of view. Some of the things I have been telling you came from the child guidance clinic people.

As far as physical health is concerned, the children who have been evacuated into the country, on the whole, are a good deal better off than they had been. The gains in weight during the fall of 1939 were considerable. That was a spurt of gain in weight which so often comes when children who have not been fed a really optimum diet are given a much better diet. The reports were that the gains in weight came early, and then after the first three or four months of living in the country, the gains sloped off and appeared to be average. The effect of going to the country on the children is apparently a very good one according to all accounts.

I think it is a matter of some interest to know where the children are in England today. I was not able to get many figures with regard to the distribution of children, for, after all, they are very busy taking care of children and don't have time to stop and study the situation, even in sufficient detail to count them and know exactly where they all are. They could tell me, however, about the school children from London. Normally in the County of London there are about 470,000 school children, but now more than four-fifths of them are already out of London. Before I left, I heard the report that that number had already been reduced and there were probably not more than 50,000 school children left.

With regard to children under 5, there were no figures that are really accurate, but it is estimated that quite a large number of children were already out in the country, either with their mothers or in what are known as nursery parties.

I do want to tell you how children are being taken care of today. The school children are practically all being taken care of all over England in individual families who have stated their willingness to take one or more children into their homes. The mothers with little children under 5 are cared for either in households where they are guests or visitors with the householder and her family, or they may be in groups in a single house together. For instance, ten or a dozen mothers and little children from a city will be placed together in one single large house, so that they either work out communal feeding for the whole group or else each mother prepares and takes care of the feeding and the care of her own children. I visited a house of that sort where ten mothers were living together, each in one room, with a little fireplace, cooking the meals for the children and herself in that one little fireplace, except for the Sunday dinner which was cooked in the common oven downstairs—a most interesting attempt to see how to take care of groups of families that needed to be moved out of a city and taken care of somewhere away from their own homes. Those mothers were very contented. They liked the arrangement. They liked it much better than being billeted, as they say, each one in a separate household.

Many of the little children under five are in nursery parties, residential nurseries. One of the first things that was done from London was to move the day nurseries in toto, or the nursery schools as a unit, out to a large house in the country. All the large houses near the big cities, especially the empty ones, were registered. They were requisitioned and taken over, and then parties of anywhere from twenty-five up to even one hundred children were moved into these houses. Staffs were employed to take care of these children. The Ministry of Health made itself responsible for the standards and regulations with respect to the care of the younger children. The Ministry also made itself responsible for the care of maternity patients. The school children were more under the general supervision of the Board of Education, although out in the rural areas, the Health Department gave advice to what were known as reception authorities in each local community, so that certain standards of care were maintained.

Some of the children had to be placed in what we call hostels; that is, one of the larger houses would be taken and a group of twenty or twenty-five children would be taken care of together. These homes were used for temporary care of children before they were placed in private households, or if the arrangements with a certain private household didn't work out very well, then the child might be placed in a temporary hostel until a new billet could be found. They were dealing with a perfectly enormous problem of child placement, and it was necessary to have certain homes to which children could be brought in transit from one individual household to another. They also have to have special homes where problem children may be cared for for a while until a proper place for them is found. They always call them "difficult children" instead of "problem children." The hostels are called "hostels for difficult children." It is a rather nice term because almost anybody could go to a hostel for difficult children and be sorted out there and sent to an appropriate place.

Before the war started, there were under construction in England what were called "school camps." It had been planned to have camps for school children for summer vacation. The school camps were immediately taken and adjusted so that they could be used as boarding schools for groups of school children, and they have been used to a great extent for special classes from London; the children who are handicapped, either physically or mentally, were sent to these special camp schools. About sixty-three of those large schools are now in use in England, each one holding about 350 children. They are not all used for handicapped children.

Some of them are used for classes of secondary school children, just like a boarding school. I visited one and found it very interesting.

The nurseries were very good. I visited eight or ten such nurseries. There was always a plan for medical supervision. As a rule, a pediatrician, or a physician in the neighborhood who was accustomed to take care of children, visited the nursery every day, or at least several times a week, and was on call for care whenever there was any need. Each nursery had a trained registered state nurse, and practically all of these nurseries had also a nursery school teacher assigned. One big nursery I visited, where there were one hundred children, had not only the state nurses and matrons and others to help care for the children, but eight nursery school teachers to help keep the children occupied and supervise the play activities during the daytime. That group was divided up into four separate groups, so that twenty-five children really lived together in four different groups in this same, very large, stately home. These are the mansions or the stately homes of England that are now filled with children and with maternity patients.

For the school children who were sick in their own homes, arrangements were made for the physicians in the local communities to take care of them, and the public authorities who are paying for this whole process of care of the children pay for that care through a pooled fund for medical service.

Children who are sick can go to two kinds of institutions. One of these is a sick bay. It is like a little infirmary for children with mild or minor ailments. I saw several sick bays, and I heard a great deal about the construction or renting or hiring of a sick bay. I don't know where the term comes from. And then the hospitals could be used for children who needed actually to be sent to hospitals. This was all worked out so that in every community where children are placed, the hospital services are available. It does not mean that in all communities there would be a children's hospital by any means, but the doctor who was in charge of the child would take the child to a hospital and the care of that child would be paid for in the hospital. For children under 5, the responsibility of paying the doctor's bill fell upon the mother, that is, if it was possible for her to pay it. Otherwise, some arrangement was made through the public assistance authorities for the medical care in those situations.

Immunization for diphtheria has taken a great spurt in England. I visited one county in Scotland where I was told they had decided this was a strategic time to get immunizations under way, and when they persuaded the local authorities that this could be done, they put on a campaign. This was a county of about 170,000 people, and on the first day of the campaign, they immunized between 7,000 and 8,000 children, and it went on until they had done a perfectly tremendous job of immunization. I think it was in less than two weeks that they immunized a large proportion of the children in the county. That is one of the things that you can do under pressure.

Throughout these various services, the influence and the help of voluntary workers are very apparent. Practically all of these hostels and institutions are staffed to a very considerable extent by voluntary workers. There are some paid workers, enough to keep the thing going, but a great deal of the work is done by women in the communities, who volunteer their time and services. There are now in England some 8,000 women who are giving voluntary service in one way or another to this civil defense effort. In these communities where children are placed, and especially the communities where mothers and young children are placed, various needs have arisen for the development of social services. You can imagine city mothers who have lived in the tenement districts of London moving out into wide open spaces in the country and not knowing what to do with themselves. They didn't know how to shop, because as a rule they were accustomed to going around the corner and buying their food at a little shop, or perhaps partly cooked already in a tin can,

Out in the country, if they had to walk two miles to go to the store, it was a very new and unusual experience for them, and one that they did not wholly appreciate.

Many adjustments had to be made in the lives of the city women who went into these country districts to live and take care of their children. When the move first took place, it did not occur to the authorities that it would be helpful if the school nurses and other health visitors from London went out to the country places and stayed in order to help the rural nurses and others in providing the services for these children. The school nurses in London at first were all turned over to the first aid units and to various other services, and it was realized suddenly that, after all, those school nurses were still needed for the same children out in the country. The doctors on the school medical staff in London, some 450 doctors, were at once discharged and allowed and encouraged to enter the Army when the evacuation first took place in 1939. Even the head of the school medical services was sent into the Army. Within two weeks of the time the evacuation took place, it was apparent that all these doctors were needed out in the country, and a lot of them back in London, because a good many children were left behind. So they had to be recalled from the Army to come back and take care of the children in the city. There is something to be learned from that, perhaps, in case of any similar need in any other country.

It was found also that the social workers who were employed by the school services in London really should have been sent out with the children to these rural areas. Again at the beginning it was decided that they would be needed more in London than in the country, but it was soon found—and it wasn't so very soon at that, within the last six or eight months—that if one of the child care workers was sent from London out to a county, or to a community in a county, many of the social and community problems which had arisen because of this sudden pouring in of strange people into a community could be solved. So today many of the child welfare workers from London are scattered all over the provinces, trying to organize in these smaller towns and in the villages some of the social services that they were accustomed to developing in the big cities. For the first time, many of the provinces in England are learning what it means to have a social worker help in the setup and the problems of the care of children and mothers.

These same community services are developing communal feeding centers. Social centers are developing where the mothers can get together in the afternoon. Children's centers, sort of nursery schools, are developing where the mothers can bring their children and leave them for a period of time. Community laundries are developing, and all that sort of thing. In this way many of the problems that have occurred in the households have been smoothed out.

I have said that there are relatively few school children left in London. Certain schools are open, and certain of the school medical clinics, which you know they have in England, are open. All of the mothers with children left in London are encouraged to bring their children to these school clinics for repeated examination and supervision. The Child Welfare Conferences in London—the Child Health Conferences, as we would call them—are open. In many cases they have been transferred now to the first aid stations, so that the health visitors and the nurses who are accustomed to handling these child health conferences may be on hand in case aid is needed. But they are going right ahead carrying out their routine child health services, using the first aid center as their headquarters. In other words, they find that they can do the two things at once. If an air raid starts, the nurses are needed for first aid, I suppose then the child health conference is given up. But the rest of the time it goes ahead as it has in the past. The same thing is happening in cities other than London. In other words, the child health conferences are now going along pretty much as they always have, and they have continued out in the rural

areas. They need additional staffs in the rural areas because, with this great influx of children, they must keep up with the service necessary in those areas.

You may be interested to know how the children are prepared medically for evacuation. I visited one of the clinics where children who were to be evacuated the next day were being examined. The school doctors and school nurses were there to give a complete examination. The examination is exceedingly careful. If there is any evidence of pediculosis, the child is sent to what is known in London as a cleansing station. Every area in London has a cleansing station. I visited one and found it filled with a number of children who were being prepared to go out to the country the next day. They have a regular arrangement by which the children go right through the mill, and it takes only one treatment to have the children in perfectly good condition to go the next day. In similar stations they give treatment for scabies and impetigo, although these conditions require more treatment. I went into one of these stations, which was a little room with shower baths all around the edge, and I think there must have been a dozen little boys, each under a shower, each provided with a large scrubbing brush with which he was scrubbing himself, with an attendant to scrub the backs. The children were then treated with some preparation of benzoin and they came back for two or three days until they were assured that the scabies were cured. Then that child is allowed to be evacuated.

There is thus a very careful procedure to be certain that the children do not carry these troublesome minor ailments which would spread through the country. Each child has a card made out by the doctor and the nurse indicating his physical status, and also something about his past history. There is indicated also whether the child suffers from a neurosis or is a behavior problem. Each child wears a tag and a comparable tag is put on his baggage. On the tag there are symbols, one of which indicates that the child is fit for billeting immediately, that he doesn't have scabies, impetigo, and so forth, and can be put directly into a home. Another symbol indicates that it would be wise if he were kept for two or three days in a temporary hostel, and the symbol indicates to the receiving officer the reason for keeping him in the temporary hostel.

You might be interested in the way in which the emergency medical services are set up in London, because it applies to the whole civilian population, and therefore applies to children quite as much as to adults. The city of London is divided into ten sectors radiating out from the center of the city, and each sector has a variety of hospitals in it, all the way from the first aid stations to the casualty hospitals to the base hospitals outside. There are two or three layers of base hospitals. Each sector has a complete medical personnel; surgeons and all the medical specialties are represented in the staff for each sector. The personnel for each sector is a complete unit and is supervised and organized by the head of this particular staff. All of the physicians who have been attending voluntary or public hospitals within that sector are assigned, according to their own specialties, to one or another of the hospitals in the sector. That means that physicians who have been attending in a voluntary hospital prior to the war may now be attending in a public hospital, or they may be attending in both. As a matter of fact, all hospitals are public hospitals at present because all of the voluntary hospitals as well as the public hospitals are under the control of the London Health Services.

In each sector there is a medical school, so that there are standards of service set up through a teaching staff in each one of these sectors. Medical teaching is going on in these medical schools just as before, but much of the clinical service now must be in the hospitals farther out, and not in the hospitals within the city. Just as fast as it is possible, patients from the center of the city are moved to the hospitals outside of the city so as to keep the beds within the city free for casualties.

What happens to children under those conditions? I went to Great Ormond Street Hospital and found that great new building of theirs had only thirty patients

in it. Some of those patients were adults, although they were mostly children. Most of those thirty patients had been there only forty-eight hours. If a patient is very ill, they may have to keep him in the hospital in town, but if the patient is not very ill, then he is moved out as fast as possible to an outlying part of the city. As a matter of fact, they were using only two wards of the hospital. Other wards were prepared for patients, but at the time I was there, there were no patients. Outside the city there are a few specialized children's hospitals, so that when a child really needs specialized care, he can be sent out to one of these hospitals.

You might be interested in what happened to some of the hospitals as a result of the bombings. At Great Ormond Street, Dr. Patterson showed me around and I saw nothing different from ordinary times. Finally he said, "Perhaps you would like to see where our bomb came through." Everybody talks about "our bomb" or "our bombs," and there is a great deal of rivalry as to whether "our bomb" did more damage than "your bomb." One bomb has hit Great Ormond Street. It is, as you know, a newly constructed building of reinforced concrete, and when a bomb hit, it went through the roof and left a hole about twelve or fourteen feet wide. It came down through the next floor, but it had to meet concrete and steel, and the force of the bomb was broken and it burst in the second floor from the top. There the blast went sideways and all the partitions of glass were broken. All the wooden partitions and plaster were down, but it was not a very serious damage. There was no damage below that point. There were no patients in the ward where it hit, so the damage was entirely physical. Except for incendiary bombs on the roof, that is all that has happened to Great Ormond Street Hospital. Let's hope that there has been nothing since I left.

I went to another hospital where a bomb had hit within forty-eight hours of the time we visited. It was an old hospital of brick, with no reinforced concrete. The result was very different. This bomb hit on one of the ward wings, a three-story ward. It hit not at the end of the ward block, but toward the corridor of the block. Half of the whole ward was down and there was just a big heap of rubble on the ground. The other half stood there and you could see the three floors standing quite separate. A good many hospitals have been hit. A good many schools in London have been hit, and of course, many of the buildings, but I may say that after all, the outlines of London are just the same as they always have been. You go about London and you see this store or this building that you recognize as of old, and certainly it seems as you wander around the streets that it is just the old London that you always knew. If you get down closely and wander around many of the streets, of course you will find many buildings out, but everything is cleaned up promptly and they are ready to go about their business exactly as usual. It is extraordinary, but that is really true.

Before I went over, everybody told us that story, you know, that it was "business as usual." Well, it really is "business as usual." It is an amazing picture of courage and high spirits and high morale in those cities in England. It is true of the children. It is true of the men and it is true of the women. It is the same everywhere.

You might be interested, perhaps, in the effect on the civil servants. I saw a good many of the civil servants, people who are doing the government work. I went into some of the offices of some of the heads of services. For instance, I went into the office of the chief medical officer in London and I was interested to see in his office, off in a corner, his bed. He has been sleeping in his office ever since last September. Many of the civil servants have just taken up their headquarters at their offices so as to be on hand. The chief medical officer is always there in case he is needed. He told me he got away for one or two week-ends, but his deputy is always on hand under those circumstances. The director of maternity and child welfare told me that for six weeks in the fall she didn't leave the office except on business. She was

there day and night. She got out early in the morning for breakfast. They ate lunch in the office, and they would get out for dinner at night, and unless she had to go out to the provinces or to do something in connection with her work, she was on the job all the time. And so it is with many of the civil servants. They are doing a really grand job. There is no discouragement. They know they have a perfectly enormous task on their hands, but they are all doing it and there is never a question of whether or not they will proceed to complete the job. And I am sure they will complete it.

You can imagine for the maternity and child health staff what it has all meant, a perfectly gigantic task to take care of their problem of moving those children and seeing that their health was protected.

I have said nothing about the maternity service. Practically all births to London mothers are taking place outside the city now, taking place in small maternity homes that have been established in these large mansions or big houses outside of London. I visited, for instance, the maternity home attached to St. Thomas' Hospital. It is in a big house twenty-five miles out of London. The head nurse and all her staff and all the equipment and all the doctors and students and interns moved right out into the country. The women register at a little prenatal clinic in town. They are seen in town as long as they stay there. They are sent out to an antenatal hostel for a month before delivery is to occur, so as to be on hand near the maternity home, and then they go to the maternity home for delivery. The standards of care are high. I visited nine or ten or a dozen of the maternity homes and they had extraordinarily good standards of care, obstetricians in attendance at every single delivery. There are two hundred such maternity homes established to serve London and some of the other cities in the southern part of England. The situation is an amazingly good response to a very great need.

DR. PHILIP M. STIMSON.—We are all enormously indebted to Dr. Tisdall and Dr. Eliot for opening our eyes to what is being done in Canada and in England, and to what we may have to do ourselves, although, of course, we all hope not.

In the last World War, the pediatrician in the Army did what he was told to do. But in this war the members of the Academy of Pediatrics have done a good deal of thinking about the situation, and it has been agreed that it is far better for the pediatricians to continue working with children. In a recent number of the JOURNAL of PEDIATRICS an editorial stresses this point very much, that it is the job of the pediatrician to work with children.

The children which we American pediatricians have to work for are in two groups. They are American children and foreign children. When this committee was started last summer, it was given the rather large title of Committee for National Defense and Relief, because it was not very definite just what was going to happen. But almost before the committee was organized there was a demand for its services for the care of refugee children from other countries. We have seen the need, also, for work with children in our own country, and steps have been started for a subcommittee on nutrition, of which Dr. Wall, of Washington, D. C., is the chairman. In a few minutes Dr. Wall will tell us what has been started and what they hope to do.

The work for children from other countries divides itself naturally into two groups, the children from England and those from the Continent. Practically all those who came over in the first month were English children. It is estimated that there were about 6,000 who came over to individual sponsors, no very accurate account being kept of them except by the British authorities. About 600 were brought over by the United States Committee for the Care of Refugee Children, and the medical needs of these children as they arrived were taken care of by volunteer pediatricians whom we have listed. There probably will be no more English children

coming over, for several reasons. I was told recently that no transportation is reasonably safe for this purpose and an attitude has developed among the children themselves in England who have stayed, scorning the children who have come over here, feeling that they have "run away from it." Parents now feel they would rather have their children stay with them and go through this period, of which Lloyd George has said that if the British Empire lives a thousand more years, people will look back at this as England's proudest hour. And the English people want their children to go through this hour with them over there.

What we can do for the English children on the other side is to see that they get proper nourishment, and it seems that one of the functions of American pediatricians is to help supply them with the needed nutritional elements.

The continental children are an entirely different proposition. The heads of all the exiled governments of the conquered countries who are in England have asked publicly that no food be sent to their conquered countries. If food is sent to their people, Germany won't have to feed them and the war will be prolonged. This applies also to unoccupied France. Germany was very canny when she made that armistice with France and had half the country occupied and half the country unoccupied, supposedly independent, but in no way independent. German commissions are all over France. Factories all over unoccupied France are working for Germany. It is said that of every one hundred tons of grain that lands in Marseilles, ninety tons goes in sealed trucks across France into Germany. If we send food to unoccupied or occupied France, the English feel very definitely that we are prolonging the war.

It is very desirable and the United States Committee for the Care of Refugee Children is very anxious to bring over children from the Continent. They have brought over about twenty-five so far through Lisbon, and about thirteen or fourteen of them were kept for a period of a month or more in a camp up in Rye, where a group of pediatricians under Dr. Higgins took care of them. Three of them were triplets, the daughters of a Viennese doctor, little girls of 13. There are great difficulties in bringing over continental children. It is necessary to have visas to cross Spain to Lisbon, which seems to be almost impossible, and they have to have transportation from Lisbon. So it is very questionable whether there will be more children coming over, even continental children. But the efforts of the United States Committee are to bring more if they can.

I would like to emphasize two or three points which Dr. Eliot made. In an English press release of a week or two ago is this paragraph: "Sir Wilson Jamieson is a well-known psychologist attached to the Ministry of Health. Sir Wilson said that England's children are bearing up admirably in the tense atmosphere created by the war. He said that only when parents display indications of nervousness do children become alarmed." We know that children are not afraid of thunderstorms until they notice their parents are afraid of thunderstorms, and the same thing apparently applies to the war condition.

This is a news release issued just today: "London, March 27th. Some of the United States' most vital aid to Britain is at work today in the English countryside. As fast as Hitler shatters the nerves of little children in Britain's 'blitzed' cities, American help is building it up again. Temporarily terrified little bomb victims are being molded into sturdy, fearless youngsters by a few weeks' country life and expert psychological treatment. In many cases the treatment takes place well within the range of Nazi bombers and scarcely twelve hours go by without the frightening wail of air raid sirens. At first the siren blasts make the babies sick and hysterical. Within a few weeks patient and understanding training has taught them not to flinch at the noise. 'It is just that "moo-cow" again,' they say. Funds from America are directly taking care of seventy babies in a small southeastern town. Two- to 3-year-old boys and girls from London's badly hit east

end were recently taken to specially prepared nursery cottages on the edge of the town. Still numb from terror, they could not eat, drink, move arms or legs, or even cry. Many had 'shelteritis,' the condition created by living so long in air raid shelters. Their eyes were full of fear and had to be shielded from the sun at first because the light almost blinded them. Their mouths drooped. Their unexercised, undernourished arms and legs were like sticks. Today they are playing in a country garden, sliding the chutes and digging in sandpits. 'A slight depression near the sandpits shows where a bomb fell a few days ago,' says the matron of one of the cottages. 'I wish Hitler could have seen our cured little bomb victims kicking the earth back into the hole next morning.' London has sent more than eighty-five per cent of the under-fives as well as the school-aged children into the country. The scheme was the constant campaign of Malcolm MacDonald, ex-Minister of Health, recently assigned to the post of High Commissioner of Canada. In one of his last interviews as minister, he said, 'We are requisitioning houses all over the country, week by week in increasing numbers. At the moment we have thousands of them being converted into family hostels, hostels for the aged and infirm, for sick children, for children under five, for working clubs, for mothers, for communal feeding centers, for maternity homes for post- and prenatal care. So far as the children are concerned, the war is not altogether an unmixed evil. Out there in the country they are thriving mentally as well as physically. This is a lesson we cannot afford to forget.' ''

There is just one more point I wish to bring up. A book has been written by an Englishwoman on the experiences and treatment of the children who were evacuated from London into the provinces. The book is called, *Borrowed Children*. Three points are brought out by the book that are worth noting. The first point is that it was highly essential right at the start to make the children feel welcome wherever they went. If they weren't welcomed, they had many more psychologic difficulties. As one little girl said, as she entered a hall where there was a great big word ''Welcome'' on a banner across the hall, it was the nicest thing she had seen since she left London, that word ''Welcome.'' The second point is that it does the children harm if they are moved from what the British call their billet, instead of being kept at the first place. It gives them a feeling of insecurity which is distinctly harmful. The third point is that children under 10, in general, did much better in private homes, while children 10 and over might very well be taken care of in larger groups, as in camps or schools or dormitories.

DR. J. F. WALL.—I am not a nutritionist, Mr. Chairman, but Dr. Stimson asked me to head the subcommittee on nutrition as a laiason officer between the Academy and those that are really nutritionists.

It so happens that we have in Washington at the present time several committees acting in an advisory capacity to the General Advisory Committee on Defense, and really reporting ultimately to Mr. Paul McNutt of the Federal Security Agency, who has these matters in charge. One of those committees is headed by Mr. Wilson of the Department of Agriculture, and another is headed by Russell Wilder, the Committee on Food and Nutrition of the National Research Council. The larger committee numbers thirty members. Nine of those members reside in Washington, and we have representation from Dr. Martha Eliot of our Children's Bureau, and Dr. Klein of the Red Cross. Twenty-one reside outside of Washington, and there are a great many skilled nutritionists on this large committee. There are also members representing agriculture and there are members representing industry, particularly the milling industry.

This larger committee has been working since the latter part of November. They have had three meetings and have really concluded, or almost completed, three bits

of work. In the latter part of November they considered the question of the enrichment of flour, and in a meeting the last of December or January, the enrichment of bread. As a result of their endeavors, I think a good many of you are seeing advertisements on bakery wagons, "Enriched Bread," whenever the bakers and millers have put back those vital ingredients, particularly the vitamins that were removed. Their third job was only partly completed by the 7th and 8th of this month, and that was concerned with standard caloric values necessary for full health and the amount of vitamins necessary for good health of adults, pregnant women, lactating women, children, babies, and adolescent children. That has not been completed and will not be until the middle of the month. Dr. Russell Wilder of the Mayo Foundation invited the chairman of the subcommittee to sit in at the next meeting on April 7, which will consider the questions of nutrition and accumulation of population, especially around powder plants, munitions works, camps, and so forth.

I would take it as the function of our subcommittee to rely, not upon any work of our small subcommittee for any investigative or research work, but to translate to the membership of the Academy the work that is done by these experts, because it would be up to the pediatricians in the several states to pass their work and their knowledge on to these men, physicians and others, who work about the camps, and that I hope we may do.

The Role of the Pediatrician in the Control of Contagious Diseases in the Army*

Philip Moen Stimson, M.D.

It may be surprising to many people to hear that contagious diseases are a very serious problem in most armies. It is generally realized that severe respiratory infections, such as pneumonia, bronchitis, and influenza can affect large numbers of soldiers, and that the venereal infections also cause the loss of an enormous amount of time, but it is not widely known that mumps, measles, scarlet fever, and diphtheria between them caused a loss of almost six and a half million days of availability of United States soldiers in the last World War. This is equivalent to putting a division of 27,000 men out of commission for nearly eight months. Mumps alone was responsible for more than half of this time, there having been over 230,000 cases in the four million men in the United States Army, with a loss of over 3,800,000 days. Of measles, there were just about twice as many cases as there were American men killed on the field of battle, and these 98,000 cases of measles caused over 2,000 deaths. Even as trifling a disease as chicken pox cost the United States Army 31,000 days. From these figures it seems obvious that there is a great deal to do in armies in the prevention and treatment of the various common contagious diseases.

It is naturally not in the American army alone that such illnesses occur. The armies of all large nations have similar troubles with these diseases. In fact, in 1918, the speaker was on duty at a British Hospital for Contagious Diseases at Rouen, in France, where at one time he had soldiers from eleven different nations as his patients in a single large ward for mumps. The British army at Gallipoli was greatly handicapped by dysentery, and all the armies in the World War were affected by the influenza epidemic of 1918.

Preventive inoculations have done wonders in lowering the incidence of some diseases which in years past have seriously crippled whole armies. For example, for each ten thousand soldiers in the United States Army in the Spanish-American War, there were 1,416 cases of typhoid fever, while in the World War the figure was less than 4, a proportionate decrease of 382 to 1. The army started compulsory vaccination against typhoid fever in 1910, and thereby saved thousands of lives.

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*Radio address, Tenth Annual Meeting of the American Academy of Pediatrics, Memphis, Tenn., Nov. 18-20, 1940.

Similarly in the case of smallpox, a well-vaccinated United States Army in the World War had, relatively speaking, one-twenty-eighth as much smallpox as the less well-vaccinated northern army in the war between the States. In 1918 some 40,000 United States soldiers were exposed to a devastating epidemic of this infection in the Philippines, that killed an estimated 100,000 natives; only thirty-four soldiers, eleven white and twenty-three native, even caught the disease, probably all men whose vaccinations were not recent, and only three of these soldiers died.

About that time in France there was an epidemic of the same virulent type of smallpox, and in the city of Rouen alone three or four hundred deaths from smallpox were said to have occurred among the unvaccinated civilian population. One night a middle-aged British tommy of the troops stationed around that city was admitted to his army's Contagious Disease Hospital, and because he had an extensive purplish eruption that looked somewhat like black measles, so-called, he was admitted to my measles ward by the officer on duty. The next morning at rounds it was apparent that this man had, not hemorrhagic measles, but hemorrhagic smallpox. His was the first case in the fifty thousand or more troops in and around Rouen, the British Army being nearly 100 per cent well vaccinated. In the twelve hours or so he was in the admitting room and in the ward, he had exposed a good many patients, stretcher bearers, and nurses, so a telephone call was put through to England for fresh smallpox vaccine. It was sent over by airplane that afternoon, and some 200 possible contacts were revaccinated that night, including myself. As a result we had no secondary cases, and altogether only six cases of smallpox occurred in the troops in and about that base.

Since the World War, advances in medical science and knowledge have enabled us to vaccinate people successfully against diphtheria. Probably 80 per cent of our soldiers then were immune, but even so there were in our army in the World War ten thousand cases of this disease, which cost 317,000 days and 177 deaths. Since then the immunization of most babies has almost wiped out diphtheria in the civilian population of many cities, but curiously enough this has apparently resulted in an increase of susceptibility among adults who are no longer stimulated to produce their own immunity by frequent slight exposures to the germs, so that today only about 40 per cent of young people are immune, or half as many as before. Unless recruits are immunized against diphtheria, an increase of the incidence of this disease in the army can be expected over that of twenty years ago.

Against measles and mumps, both serious causes of great loss of time to armies, we have as yet no method of vaccination or long-term immunization. However, in the last few years it has been learned that the blood serum of people who have had these illnesses does protect exposed persons for a short time, and it would seem highly desirable for the army to establish blood banks of convalescent serum to protect against measles and mumps, even as blood banks are being established to provide adequate treatment of shock due to war injuries. If each army camp had a convalescent serum bank, particularly those camps that draw their recruits largely from rural areas, then on the occurrence of the first cases, the exposed susceptible men could at once be given protective doses of the serum and epidemics could be held to a minimum.

The problem of contagion in an army varies greatly with the source of the troops. Young men who have grown up in cities have been exposed to most of these diseases and have built up somewhat of an immunity either by an attack of one or more of the infections or just by frequent exposure. But boys who have grown up in backwoods districts, on farms, or in other rural communities have usually never been exposed to any such infections, and when thousands of these rural young men are first massed together in army camps, contagious diseases are apt to be very common. Therefore, in 1918 some army camps actually had relatively 100 times as many cases of a disease as did other army camps. It is in the hospitals of such camps where pediatrists can be useful.

In civilian life the contagious diseases occur, in the great majority of instances, in children, and it is the children's specialists or pediatrists who have most experience in the prevention and treatment of this particular group of maladies. In recent years there has been a slight tendency for the illnesses to be relatively more common in adults, perhaps because more and more children are receiving preventive inoculations.

As soldiers are now being assembled by tens of thousands in army camps, there is much to be done to spare them from unnecessary illness. Immunizing vaccinations must be performed, proper sanitary conditions must be arranged and preserved, adequate preparations made to handle epidemics, and well-trained clinicians provided to care for the men when sick. In all these aspects of military medicine, pediatrists can prove useful medical officers.

As a matter of fact, the control of contagion devolves on a number of different kinds of experts—on public health and sanitation workers, on laboratory investigators, and on clinicians, both internists and pediatrists. Various of the pediatrists can qualify in several of these categories and have done so in times past.

It is particularly essential to have skilled diagnosticians available to make sure that the illnesses are correctly diagnosed. The caliber of doctor in the United States Army Medical Corps is very high, but during the World War, when thousands of civilian doctors were added to this corps, sometimes less than perfect efficiency resulted. For instance, statistics show that eighty-two soldiers died of supposed German measles, of which over 17,000 cases were diagnosed. Now most people know that a death from German measles is an exceptional rarity, if it ever occurs, and it is of interest to note that most of these thousands of cases and eighty-two deaths were reported from army camps in which relatively little scarlet fever was recorded. It is sometimes very difficult to distinguish German measles from scarlet fever, as well as from true measles, but trained pediatrists are perhaps best equipped to make this differentiation.

The British had consultants for just such diagnostic problems, but even they sometimes had their troubles. One such medical colonel used to visit the contagious disease hospital at Rouen every Wednesday afternoon. One week he was quite caustic because that morning a case had been found newly admitted to the scarlet fever ward which had later been diagnosed as German measles. The patient was being moved out as the colonel came by. Even while he was scolding the medical officers involved, the admitting officer of the day appeared and asked for the consultant's opinion on a new case at that moment in the admitting room. It proved to be a tommy with an indefinite rash that could have been almost anything, one about which anybody could guess right or wrong. The consultant looked him over quite carefully, hemmed and hawed, and finally roared out, "Well, you'll just have to do the best you can," and stalked away. Perhaps pediatrists would not have found it any easier to diagnose, but they constantly have problems of that sort to solve.

In the United States Army in the World War, pediatrists were enrolled in great number, but comparatively few had opportunities to work on the contagious diseases. Of the others, one man became the commanding officer of an army base hospital in France. At least two were adjutants of base hospitals. Many were regimental medical officers or staff officers in various military hospitals, and many more worked for civilian relief.

Army authorities naturally endeavor to place each man in some field of activity where his training and abilities have fullest scope, and naturally pediatrists are more suitable for work in connection with the prevention and treatment of the common contagious diseases than for any other sphere of military medicine. However, in the present emergency, even as during the World War, the pediatrists of this country will undoubtedly show themselves . dy to accept any military assignment given them, and will do the best they can.

News and Notes

Dr. Fred Moore of Des Moines, Iowa, a founder member of the Academy, died April 8, 1941, of gastric carcinoma. In addition to an active pediatric practice, Dr. Moore for many years had been director of School Health Service in Des Moines, and his work in this connection had gained national reputation. From 1931 until his death he was a member of the House of Delegates of the American Medical Association, and since 1934, a member of the Council on Medical Education and Hospitals.

The dates of the October examination to be held in Boston by the **American Board of Pediatrics** have been changed to October 7 and 8. These are the two days preceding the annual Academy meeting, in place of the two days following the meeting, as previously scheduled.

The **Second American Congress on Obstetrics and Gynecology** will be held in St. Louis, Mo., April 6-10, 1942. The general plan for the program will be much the same as that of the first Congress, which was held in Cleveland, Sept. 11-15, 1939, with sectional meetings for the various groups (nurses, public health administrators, educators, and physicians), general sessions for all members attending the Congress, and round tables. Evening sessions will be open to the general public.

Book Reviews

Cardiac Classics. Fredrick A. Willius, M.D., and Thomas E. Keys, M.A. St. Louis, 1941, The C. V. Mosby Co., pp. 858. Price $10.00.

Dr. Willius, chief of the Section of Cardiology, and Mr. Keys, reference librarian of the Mayo Clinic, have selected a group of fifty-two classic works on the heart and circulation by fifty-one authors. Each classic is preceded by an excellent biography of the author, accompanied in most instances by a photograph. Starting with William Harvey's "On the Motion of the Heart and Blood in Animals," published in 1628, the volume ends with James Herrick's "Clinical Features of Sudden Obstruction of the Coronary Arteries," published in 1912. It is impossible to include a list of all the classics, but such names as Malpighi, Heberden, Morgagni, John Hunter, Corrigan, Stokes, Austin Flint, His, Broadbent, Einthoven, and Mackenzie suggest the type and scope of the classics selected by the authors. It is an extremely important collection not only to the cardiologist, but to every physician interested in his profession, covering as it does a period of three hundred years of medical progress and development. The book is excellently printed, and the numerous illustrations and photographs have been carefully selected.

Health Education. National Education Association, Washington, 1941, pp. 368.

This is the second revision of the guide for teachers prepared by the Joint Committee on Health Problems in Education of the National Educational Association and the American Medical Association. The original report appeared in 1924 and a revised report in 1930. Experience, new knowledge of methods, and, above all, scientific progress have necessitated this new revision. The material has been carefully revised and studied and checked by experts in special fields. It contains a mass of material and factual data on health trends, nutrition, hygiene in special fields, methods of instruction, etc., all clearly and simply stated. As in the past, the book will continue to hold its place as the standard text on health education. An excellent bibliography of nearly fifty pages lists under appropriate headings all of the important source material to date, for those who wish to go further into some particular phase. Dr. Charles C. Wilson is chairman of the Joint Committee. The report has been arranged and edited splendidly by Miss Anne Whitney.

Feeding Our Old-Fashioned Children. Anderson Aldrich and Mary M. Aldrich, Macmillan Co., New York, 1941, pp. 112. $1.75.

Dr. Aldrich started to revise his earlier book, "Cultivating the Child's Appetite," but found that time had brought about many changes, and this new book is the result. The volume clearly presents the changing trend of thought of modern pediatrics in simple, nontechnical language, and can be recommended to parents who are faced with the problem of anorexia, or even better where the pediatrician recognizes the probability of such a problem's arising. Fundamentally, the theme is to consider the child and not questions of food. The physiology of eating and the psychology of appetite are first discussed and then the question of problems. Occasional brief case histories are used to drive home the point the authors are making. Considered together with "Babies Are Human Beings," which was reviewed in these columns

a couple of years ago and which has had a well-deserved success, these two books by the Aldriches are the most understanding and satisfactory books on the phases of child care which they consider that are available for parents.

Growing Out of Babyhood: A Handbook for Parents on the Problems of the Preschool Child. William S. Sadler, M.D., and Lena R. Sadler, M.D., Funk & Wagnalls Co., 1940. Price $2.50.

The reviewer must confess that he approached this book with misgivings and some prejudice. The authors have previously published books with naïve titles of an alarming lure to the uninformed and trusting reader—"The Mind at Mischief," "Piloting Modern Youth," "The Quest for Happiness," "Mastering Worry and Nervousness," etc. This is something of an array of puzzles, the solution of which would need wisdom, information, experience, and knowledge scarcely within the limits of the human mind, even though these minds belong to psychiatrists. Reading the opening chapter and further along served to dissipate the reviewer's preformed opinion of this book completely. It is full of common sense and good advice. A sentence from the preface is worth quoting as it seems the guiding pattern of the authors' attitude to the problems included in the title: "We have endeavored to steer a middle-of-the-road course between the austere physiologic psychology and the overemphasis of the importance of affording the child a full feeling of security in the parental affection, and we believe it is possible to carry out a commonsense program in child training which avoids both of these evils." This is a fine attitude and it is followed out in the book in dealing with the many problems which it attempts to clarify and furnish guidance for.

There is a good-humored skepticism concerning the all-or-nothing interpretation of such things as play, temper tantrums, thumb-sucking, feeding difficulties, etc. These in the hands of the rigid analytical psychologic school tend toward generalizations as to causation and future fate which may have frightening implications to the innocent father or mother. The authors do not believe that play is an attempt only to prepare for the activities of adult life. It is something of that, plus a great deal more and a great many more simple things. It is energy, enjoyment, adventure, imagination, imitation, and a pleasant way to express oneself. All these and many others are involved and there is no one category into which play fits.

Parents may be of aid to their children in the play activity, for example, if they can regard play from several points of view instead of one. If they have an idea that play is merely a preparation for life, their assistance, participation, and observation of their child at play will very likely be limited with that one idea in mind. The more general and generous the interpretation of play becomes, the more will the parents be able to view the play of their children as serving many purposes, many of which could easily come within the scope of their understanding and guidance. This is simply one example of how necessary it is to regard the activities of the child from a broad rather than a narrow point of view. This illustrates also the manner in which authors approach the behavior problems presented by children.

The book is good reading and is not too authoritative, and the description of what the child does and how much trouble he causes for the reason that he is a child is easily within the grasp of intelligent parents. It is put down as clearly as it can be made and as usefully as experience shows.

Child as well as adult behavior is an intricate matter to interpret. Dogmatic assertions are out of place in either category. In children, however, something can be done on the spot. Intelligent parents not too confused by the interplay of theories

originating in adult minds, and often by people pretty remote from the child, at least one's own child, are the ones to carry out what the situation demands. This book will show a way, and not much more can be expected from any book of this kind.

The reviewer is glad to admit that he was pretty wrong when he began to read this book and that he is glad that he did read it, and now he recommends it to others. A book that can change a preformed opinion is, one would say, a book worth while.

Science and Seizures. William G. Lennox, M.D., Harper Brothers, New York, 1941.

This book has been long in the making and eagerly awaited. Lennox's interest in the problem of epilepsy has become established both by his popular and technical papers and by his pioneering effort in the problem and social aspects of this disease. He frankly wants to place at the service of the epileptic, his family and friends, and the public generally his own knowledge of this disease and the information which he has derived from his experimental and clinical research and that of his coworkers. This he has done admirably in this book. He has mastered the art of writing on a technically intricate medical subject so that a nonmedical reader may not only understand but may be interested. The directness and simplicity of style required for the easy dissemination of information to people in general are evident on every page of this book and in the consideration of every phase of the problem of epilepsy touched upon, and there is nothing of importance omitted and unemphasized.

The final chapters deal with migraine. In a popular book on epilepsy this might seem a questionable inclusion as headaches are so widespread that the average reader might well be confused as to the relation between so common a condition and so dreaded a disease as epilepsy. The connection between these two is established on rhythm and periodicity rather than on similarity of origin and causation. In this way the reader is impressed by the evidence of the biologic characteristic of "nature itself, the ebb and flow, growth, decay, calm and storm, peace, war, life and death—an alternating rhythm (purposeful dysrhythm) of the Universe." This is an example of Lennox's ability to state so simply and convincingly an eternal truth which finds its application to both epilepsy and migraine, without forcing the issue of a common and shared causation, clinical expression, or common fate.

The book can be read with profit by physicians as well as laymen. It is interesting and so well arranged that the complete subject of epilepsy becomes a well-integrated picture, its wholeness not interfering with the clear appreciation of the identity of its parts. The factor of heredity on the basis of a widespread and fairly common demonstration of cerebral dysrhythmia as shown by the electroencephalogram is convincingly shown. It is scarcely necessary to state that the author is not dogmatic on the subject of inheritance of epilepsy in spite of what he apparently regards as pretty definite proof. The diagnostic criteria, the use of drugs and other therapeutic measures, the social implications of the individual with epilepsy, marriage and eugenics, prophylaxis, all this and many other parts of the epileptic problem are touched upon with the same thoughtful, careful, and simple manner characteristic of the author's attitude towards the subject which he has selected as his chief object of study, research, and experiment. With a rare spirit of social sensitiveness, Lennox has wished to share what he knows about epilepsy with the people who have this disease, with the family and friends who share its burden, and especially with the physicians whose patients they become. This is a fine book, beautifully arranged and written for its purpose, and it should be in the hands of all those whom epilepsy even remotely touches.

Schizophrenia in Childhood. Charles Bradley, M.D., Macmillan Co., New York, 1941.

This book is an attempt to establish the fact and rarity of schizophrenia as a clinical entity in the age incidence of childhood. Childhood is defined here as "the immature child prior to the onset of physiological puberty . . . childhood is clearly demarked from adolescence and from later adult life." The survey of the literature on schizophrenia is well done, and the quotations from case reports as they serve to illuminate some of the psychopathologic features of this mental disease are of great service to those who have only a vague notion of what the term schizophrenia means. A good picture of adult schizophrenia evolves from the historical survey from the Kraepelin period to the present time. Perhaps this is the most valuable part of the book.

According to the author, childhood schizophrenia is considered a rare but severe disturbance of the personality characterized by a diffuse retraction of interest from the environment. There is a diminution of affective contact with reality, loss of interest in the surroundings, failure to derive emotional satisfaction from the ordinary events of life, and preoccupation with subjective matters to the exclusion of external situations. He adds this statement which is the key to the situation: "Since young children have not yet developed the capacity to express their mental content verbally, criteria for schizophrenia at this age are mainly on the behavior level." The reviewer would add—nor have they the capacity to organize the framework of their own personality in a subjective sense in relation to the external world and to the field of experience. If such a statement is valid, then the essential difference between childhood and maturity in relation to the mechanism of schizophrenia as it is known in the psychiatric sense is clear. The development of this disease as a broadly outlined clinical entity raises the question of the possibility of the occurrence of schizophrenia in childhood and makes it difficult to identify or even to conceive it.

The case reports, including the author's own material, are interesting and well done descriptively. They establish the fact of behavior situations and reactions which observationally are not essentially different from those seen in adult life. To designate these cases as childhood schizophrenia makes little difference in the long run, but it is difficult to see what advantage toward a better understanding of these puzzling psychoses would result.

Schizophrenia is becoming a vague descriptive outline of personality and behavior disturbances with a background of conceptional and emotional distortion which tend toward recessive drives and toward childish and infantile patterns. The paradox is here apparent. If a certain degree of maturity is necessary for the recessive trend to take place, then how can the immaturity of childhood lay the necessary foundation for such changes. Schizophrenia is dependent upon the difficulties and conflicts of living and the individual's incapacity to adjust to this essential fact. One has to live long enough to experience these things in order to carry out the mechanism implied in schizophrenia. Childhood, among other things, has not lasted long enough in time.

In spite of the fact that childhood schizophrenia does not come out of this book as an established fact nor as a well-crystallized clinical entity, and if the main thesis is not convincingly proved, yet it remains a worth-while attempt to focus upon behavior abnormalities in childhood the conceptions that have developed in adult schizophrenia. The book is well written and very well organized. The literature references are of permanent value.